The effect of three different cooling gels on acute non-specific low back pain

By

Cleo Kirsty Prince

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I, Cleo Kirsty Prince do declare that this dissertation is a representation of my own work in both conception and execution.

Signed: _____ Date: _____

C. K. Prince

Approved for final examination

Signed: _____ Date: _____

Dr. L.M. O' Connor

MTech: Chiropractic

Supervisor

Signed: _____ Date: _____

Prof. D. Gerber

BVSc, Dr.med.vet

Co-Supervisor

DEDICATION

This dissertation is dedicated to:

My Lord and Saviour Jesus Christ

Who makes all things possible in His time

To my Mum and Dad, words cannot express the eternal gratitude I will always have for the two of you for helping me pursue my dreams. The countless sacrifices and hard work that you have put towards my education is the greatest gift you could have ever given to me. Thank you for being mentors, confidants and role models.

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ABSTRACT

Background

Cryotherapy is often the first option in treating acute conditions and can be applied in various forms including ice packs and cooling gels. Cooling gels are easy to use and readily available making them popular with consumers. They can also contain additional ingredients which can assist with inflammation, making them ideal for musculoskeletal disorders. A cooling gel containing menthol and anti-inflammatory herbs is available in pharmacies nationwide in South Africa, but has not been clinically investigated. This gel is often used in the treatment of acute injuries such as low back pain but its effectiveness in treating this condition has not yet been verified.

Objectives

To determine the effectiveness of a menthol cooling gel combined with anti-inflammatory herbs compared to a menthol gel and a placebo gel in the treatment of acute non-specific low back pain.

Method

A double-blinded placebo controlled clinical trial (n = 60) was conducted. Each participant was randomly allocated into one of three treatment groups consisting of a minimum of 20 participants between the ages of 18 and 40 who met the study criteria. Informed consent was obtained from the participants prior to their participation in the study. At the initial consultation baseline measurements (pain rating, disability and pressure pain threshold) were taken and the respective treatments (menthol with anti-inflammatory herb, menthol or placebo gel) were administered. Participants were instructed on how to apply the gel at home and were requested to apply it three times a day for one week. Statistical analysis was performed using repeated measures ANOVA for inter- and intra-group analysis with one way ANOVA and chi square tests being used to compare baseline values. A p-value < 0.05 was considered to be statistically significant. The study received ethical

clearance from the Durban University of Technology Institutional Research Ethics Committee (REC 81/13).

Results

No significant differences were observed between the groups at baseline assessment, indicating that the groups were comparable. Participants were instructed on how to apply the gel at home and were requested to apply it three times a day for one week. Follow up appointments for data collection was scheduled at days three or four and six. No statistically significant differences were observed between the three groups over time for pain ($p = 0.95$), disability ($p = 0.903$) or pressure-pain threshold ($p = 0.824$), with all groups showing improvement. All three groups showed clinically significant changes in pain from moderate to mild over the duration of the study but no clinically significant changes were noted in terms of pressure-pain threshold and disability.

Conclusion

The results indicate that irrespective of whether or not the gel contains active ingredients there was an improvement in acute low back pain. Further research needs to be conducted to determine if tissue depth and the concentration of the active ingredients such as menthol are factors affecting the efficacy of this gel.

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CHAPTER ONE: INTRODUCTION

1.1 The problem and its setting

Low back pain (LBP) is defined as pain in the lumbosacral region which may radiate to the buttocks and thighs (Kinkade, 2007; Walker, 2012); it is a common complaint with 80% of the world's population experiencing at least one episode of low back pain in their lifetime (Chiodo *et al.,* 2005). Due to its high prevalence, low back pain is a major cause of disability, leading to absenteeism from work which results in a loss of productivity, and a significant impact on the economy of a country (Hanney *et al.,* 2009). Low back pain may be either mechanical in nature which makes up the vast majority of low back complaints (97%) or non-mechanical (3%) where the aetiology could be from a specific cause such as cancer, infection and inflammatory arthropathies (Atlas and Deyo, 2001; Diamond and Borenstein, 2006). Mechanical low back pain is defined as pain arising from an injury to or malfunctioning of the structures within the spine (Walker, 2012) and is often aggravated by activity and loading of the spine, whereas pain is relieved by rest (Dagenais and Haldeman, 2012).

Low back pain can be defined as either acute, if it is present for less than two weeks or chronic if present for more than 12 weeks (Atlas and Deyo, 2001; Chiodo *et al.,* 2005; Balagué *et al.,* 2012). Acute LBP is usually self-limiting (Chien and Bajwa, 2008), resolving within two to four weeks without treatment (Hills, 2012), but in 10 to 15 percent of individuals it may progress to the chronic stage, which often presents as a greater challenge to treat (Balagué *et al.,* 2012). In the acute stage the patient may present with pain and disability possibly due to the formation of oedema and inflammation associated with local muscle spasm (Bronfort *et al.,* 2010).

Cryotherapy, the therapeutic application of cold (Swenson *et al.,* 1996), is often the first option in treating acute conditions (Bleakley *et al.,* 2006). Its physiological effects such as the reduction in tissue temperatures results in vasoconstriction of the local blood vessels leading to decreased oedema and a reduction in tissue damage

(Bleakley *et al.,* 2006). This sequentially has a positive effect on pain relief and recovery (Best, 1997). There are many methods of applying cryotherapy each with its own thermodynamic properties resulting in different cooling efficacies (Merrick *et al.,* 2003). This together with practical considerations may influence a manual therapist's decision to use a particular modality.

Traditionally cryotherapy is applied in the form of an ice pack however many practitioners and patients are utilizing cooling gels. Cooling gels have an advantage over traditional ice packs in that they do not require refrigeration, can be portable and are easily accessible (Airaksinen *et al.,* 2003). The majority of cooling gels contain menthol as a primary ingredient (Topp *et al.,* 2011) which, when applied topically, produces a 'tingling' sensation and a feeling of coolness due to the stimulation of cold receptors on the surface of the skin (Galeotti *et al.,* 2002).

Menthol has been found to enhance the penetration of ingredients such as topical anaesthetics (Liu *et al.,* 2005), therefore making it beneficial to include other agents in menthol gel formulations. Menthol reacts with the intact skin and may disturb the barriers to penetration of exogenous materials, making the skin more permeable and thus the ingredients combined with menthol are able to be delivered transdermally (Karande and Mitragatri, 2009). These additional ingredients are often added to aid healing during the inflammatory phase, and may make them more appealing to people suffering with musculoskeletal disorders such as low back and neck pain. Added benefits of cooling gels are that they are easy to apply and patients are able to administer the gel themselves as part of a self-management strategy which could assist the patient in playing a role in their own return to health. However their effectiveness is not well documented.

The cooling gel that is available in pharmacies across South Africa contains menthol, Arnica, Echinacea and a combination of anti-inflammatory herbs. The cooling gel is popular amongst people with musculoskeletal injuries (Gerber, 2013); however there is limited research on the effectiveness of this gel to treat musculoskeletal conditions. In participants with acute ankle sprains, Harper (2010) found that this gel was as effective as an ice pack and a plain menthol gel in reducing pain, oedema, and disability and resulted in increased pain thresholds, with the three interventions

being superior to a placebo intervention. Although this study supplies some evidence to support the use of this cooling gel, the ankle joint is relatively superficial when compared to areas such as the low back, which has a significantly greater tissue depth. Thus the necessity to further investigated this gel's efficacy in various other parts of the body. Additionally as very little benefit was seen to be derived from the addition of anti-inflammatory herbs to the gel in Harper's study (2010), additional research is necessary.

1.2 The research question, study aims and objectives

1.2.1 The research question

What role do cooling gels have in the management of acute non-specific low back pain?

1.2.2 The aim

The study aimed to compare the effect of three gels; a menthol cooling gel with anti-inflammatory herbs, a menthol cooling gel and a placebo gel, on pain, disability and pain tolerance associated with acute non-specific low back pain in individuals residing in the greater eThekwini municipality.

1.2.3 The study objectives

Objective One:

To determine the effect of a menthol cooling gel containing anti-inflammatory herbs on pain, disability and pain tolerance in participants with acute non-specific low back pain.

Null Hypothesis (H_o) One: There will be no statistical significant improvement ($p>0.05$) in pain, disability and pain tolerance on the intra-group analysis for participant's with acute non-specific low back pain receiving the menthol cooling gel containing anti-inflammatory herbs

Alternate Hypothesis (H_1) One: There will be a statistically significant improvement ($p<0,05$) in pain, disability and pain tolerance in participants with acute non-specific low back pain receiving the menthol cooling gel containing anti-inflammatory herbs.

Objective Two:

To determine the effect of a menthol cooling gel on pain, disability and pain tolerance associated with acute non-specific low back pain.

H_o Two: There will be no statistical significant improvement ($p>0.05$) in pain, disability and pain tolerance on the intra-group analysis for participant's with acute non-specific low back pain receiving the menthol cooling gel .

H_1 Two: There will be a statistical significant improvement ($p<0.05$) in pain, disability and pain tolerance in participants with acute non-specific low back pain receiving the menthol cooling gel

Objective Three:

To determine the effect of a placebo gel on pain, disability and pain tolerance associated with acute non-specific low back pain.

H_o Three: There will be no statistically significant improvement ($p>0.05$) in pain, disability and pain tolerance on the intra-group analysis for participant's with acute non-specific low back pain receiving the placebo gel

H_1 Three: There will be a statistically improvement ($p<0.05$) in pain, disability and pain tolerance in participants with acute non-specific low back pain receiving the placebo gel

Objective Four:

To compare the effect of the three gels on pain, disability and pain tolerance associated with acute non-specific low back pain

H_o: There will be no statistically significant improvements ($p>0.05$) in pain, disability and pain tolerance between the three groups.

H_1 Four: The group receiving the menthol cooling gel containing anti-inflammatory herbs will show a statistically significant improvement ($p<0.05$) in pain, disability and pain tolerance when compared to the menthol and placebo gel groups

1.3 The flow of the dissertation

Chapter One has outlined the context of the research problem and the aims and objectives of the study. This will be followed by Chapter Two where a review of the literature relevant to the research problem will be presented. Chapter Three outlines the methodology which was utilized in this study with Chapter Four that provides the results of statistical analyses. Chapter Five discusses these results and critically analyses them in relation to the available literature, and Chapter Six presents the conclusions and recommendation

CHAPTER TWO : LITERATURE REVIEW

2.1 Introduction

Non-specific low back pain has become a public health concern worldwide (Balagué *et al.,* 2012) and affects approximately 90 percent of the population at some point during their lifetime (Brennan, 2007). Most cases of low back pain are mechanical, thought to arise from dysfunction of the anatomical structures within the lumbosacral region (Chien and Bajwa, 2008). If left untreated, in 10 to 15 percent of patients the condition may progress to the chronic stage (Balagué *et al.,* 2012). Thus an effective management strategy is required to prevent this condition progressing. Cryotherapy is often used by patients and practitioners as an initial treatment for acute conditions such as low back pain (Wright and Sulka, 2001; Bleakley *et al.,* 2004). This chapter will provide a review of the literature regarding the anatomical structures that contribute to acute low back pain, the underlying mechanism of the condition and its management with particular emphasis on cryotherapy and cooling gels.

The information gathered in this chapter was sourced from the available scientific literature on MEDLINE (pubmed), EBSCOhost, Proquest and the Springerlink databases. The following key search terms were used; skin, mechanical low back pain, cryotherapy, cold, cooling gels and menthol, to obtain literature relevant to this topic**.** No limitation was placed on the year of publication of the available literature and only literature written in English was analysed and discussed.

2.2. A brief overview of the anatomical structures of the low back

When discussing low back pain it is important to identify the various structures that may be involved, therefore a brief overview of the bony anatomy and soft tissue of the low back is presented.

2.2.1 The bony structures of the low back

The low back region consists of the lumbar spine which is made up of five vertebrae, named L1 to L5. Each vertebra consists of a kidney-shaped body, a neural arch and seven bony processes (Kishner, 2014), as illustrated in Figure 2.1.

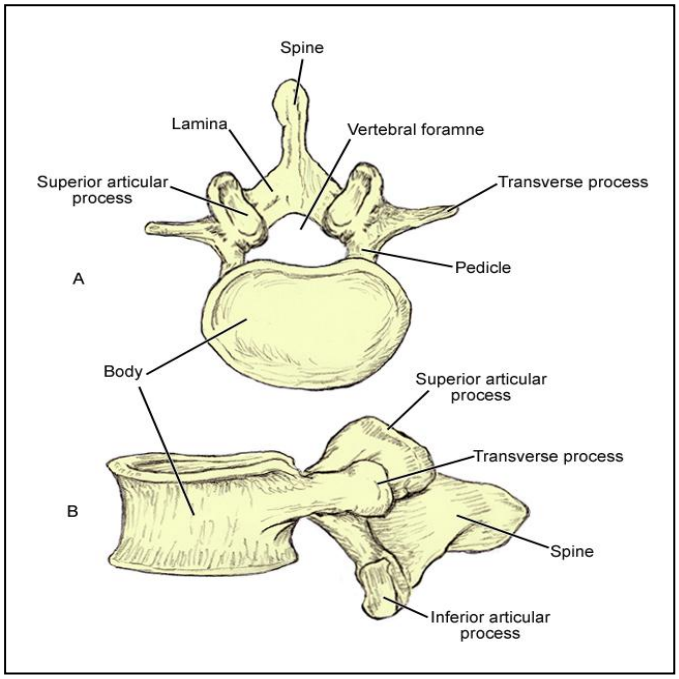


Figure 0.1: The Bony Structure of the Lumbar Vertebra
(Kishner, 2014)

Each vertebra articulates with the next through two zygopophyseal joints, commonly known as the facet joints, one on each side of the vertebrae as well as through the intervertebral disc (IVD) (Kishner, 2014). The facet joint is formed by the superior articular process of one vertebrae and the inferior articular process of the vertebra above (Laub, 2008). The posterior branches of the lumbar artery (Gilchrist *et al.,* 2002) supply this joint and it is innervated by the medial branch of the dorsal rami of the spinal nerves (Malanga, 2011). The facet joints are required to withstand large amounts of stress from the body and are often subjected to acute and repetitive injuries which may lead to degenerative arthritis (Laub, 2008). Pain may originate from these structures due to degenerative or inflammatory processes within the joint itself or from any outgrowth from the joint which may impinge on nearby structures; referred to as facet syndrome (Malanga, 2011).

The IVD is situated between the endplates of successive vertebrae (Laub, 2008) and acts as a cushion to absorb forces disseminated throughout the spine, to protect the facet joints from excess forces, and to allow for movement between the vertebrae (Laub, 2008; Shankar *et al.,* 2009). The IVD is innervated by the sinuvertebral nerve, the anterior primary division and the gray communicating rami of the sympathetic chain. It receives its arterial supply from the segmental arteries which supply the

vertebral bodies and endplates of the disc. The blood supply is however limited to the outer annulus fibrosis, thus the nutrition of the disc itself relies on the bulk movement of fluid in and out of the disc to transport nutrients (Shankar *et al.,* 2009). If the IVD is damaged, the inner gel-like disc material, the nucleus pulposus, may push through the annulus fibrosis, and cause a disc bulge or herniation. This may result in sharp, severe low back pain (Baldwin, 2014).

At the base of the lumbar spine there is a large, triangular and wedged-shaped structure called the sacrum. It is composed of five fused sacral vertebrae and at its distal end is the coccyx. The sacrum provides strength and stability to the pelvis and transmits the weight of the body to the pelvic girdle (Moore and Dalley *,* 2005). The sacrum articulates with the ilium of the pelvic bone, forming the sacro-iliac joints (SIJ) (Laub, 2008). The SIJ functions to transmit forces between the trunk, spine, lower limbs and the ground (Vleeming *et al.,* 1998). They receive their arterial supply by means of the median sacral artery (Lyons, 2011). Innervation of the posterior aspect is via the lateral branches of the posterior rami of L4 to S3 and of the anterior aspect is via the lateral branches of the posterior rami of L2 to L3 (Bernard and Cassidy, 1991). Mechanical dysfunction, inflammation, infection, trauma and degeneration may cause pain within these joints, which is known as sacroilliac joint dysfunction (Sherman, 2014).

2.2.2 Soft tissue structures in the low back

The ligaments of the lumbosacral region, as outlined in Appendix A, are strong fibrous soft tissue structures which firmly attach bone to bone (Shiel, 2014). Their role is to passively stabilise joints and aid in guiding these joints through a normal range of motion when a tensile load is applied and also play a role in proprioception- the conscious perception of the positioning of the limb in space (Frank, 2004). Ligaments are often torn or stretched in traumatic joint injuries, leading to partial or complete ligamentous tears (Frank, 2004), which will present with low back pain in the area of damage (Nestor and Sheidler, 2008).

Another common source of low back pain is from the musculature of the low back. These muscles are categorised into either extrinsic or intrinsic back muscles. The extrinsic muscles allow for global movements of the trunk and extremities while the

intrinsic muscles are located deep and assist in maintaining posture and movements of the vertebral column (Comerford and Mottram, 2001). The intrinsic muscles are further divided into superficial, intermediate and deep layers as seen in Appendix B. Damage to the musculature as a result of performing sudden or forceful movements or by improper lifting of a heavy object, may lead to muscle strain, resulting in pain in the low back or upper buttocks area (Cluett, 2014).

2.2.3 Vasculature of the low back

The first four lumbar vertebrae, surrounding musculature and ligaments are supplied by the branches of the right and left lumbar arteries, which are four paired segmental arteries arising from the posterior lateral aspect of aorta (Gilchrist *et al*, 2002). The skin overlying the low back is supplied by cutaneous blood vessels (Demarchez, 2011). The epidermis contains no blood vessels and depends on the underlying dermis for nutrition and the removal of waste via diffusion through the dermal-epidermal junction (Amirlak*,* 2013). The dermis and hypodermis are supplied by two intercommunicating arterial plexuses (Kolarsick et al., 2011).

A small unpaired artery, the median (middle) sacral artery, supplies the sacrum (Cramer and Darby, 2014). Along its course, it gives off a small branching blood vessel to supply the L5 vertebra (Gilchrist *et al*., 2002) and transverse lateral branches which anastomose with branches of the lateral sacral artery, a branch of the internal iliac artery, to supply the sacrum and muscles of the pelvic floor (McMurrich and Sobatta, 2000).

The veins which surround and drain the vertebrae, associated muscles and ligaments and the skin of the lumbar region of the spine include the lumbar veins, the ascending lumbar veins and several vertebral venous plexuses. The lumbar veins accompany the lumbar arteries in their course around the vertebral bodies and drain into the ascending lumbar vein, which in turn communicates with the common iliac vein inferiorly on each side. Superiorly, the right ascending lumbar vein joins the azygous vein and the left ascending lumbar vein joins the hemiazygous veins which both in turn drain into the inferior vena cava (Bogduk, 2005). The overlying dermis is drained by the venous subpapillary plexus which in turn will drain into the small veins of the subcutaneous plexus which then drain into regional cutaneous veins and empty into the inferior vena cava (Imanishi *et al.,* 2008).

The venous drainage of the sacrum follows an arrangement similar to that of the arterial supply (Kelley and Peterson, 2007). The median and lateral sacral veins accompany their respective arteries and drain into the internal iliac veins which unite with the external iliac veins to form the common iliac veins, which then unite at the level of L4 to form the inferior vena cava (Moore and Dalley, 2005).

2.2.4 Innervation of low back

The musculature, ligaments and vertebrae of the lumbar region are innervated by the lumbar spinal nerves which lie within the intevertebral foramina and are numbered according to the vertebrae under which they lie. These nerves are connected to the spinal cord by dorsal (sensory) and ventral (motor) nerve roots and divided into dorsal and ventral rami on exiting the intevertebral foramina (Bogduk, 2005). Similarly, the sacrum and its surrounding structures are supplied by five sacral nerves that arise from the sacral foramina (Stedman, 2005). The innervation of the skin is supplied by the medial and lateral cutaneous nerves and anterior and posterior cutaneous nerves, arising from the dorsal ramus and anterior ramus, respectively, which are branches of the spinal nerves, exiting at each vertebral level (Standring, 2008).

2.3 Low back pain

Low back pain is defined as pain which presents posteriorly in the area between the lower rib margin and the proximal thighs (Kinkade, 2007). The majority of low back pain is mechanical in origin (97 percent) with about three percent of cases being non-mechanical in nature (Diamond and Borenstein, 2006; Chien and Bajwa, 2008).

2.3.1 Epidemiology of low back pain

Epidemiological studies have found that the point prevalence of low back pain ranges from 15 to 30 percent, with the one year prevalence being 50 percent (Dagenais and Haldeman, 2012) and a high lifetime prevalence of 50 to 80 percent (Chiodo *et al.,* 2005; Dagenais and Haldeman, 2012). A cross-sectional random survey (n = 355) determining the incidence and prevalence of low back pain within the South African workplace, found the six month prevalence to be 41 percent, the lifetime prevalence to be 63 percent and the point prevalence to be nine percent (de Wet, 2003).

Due to its high prevalence, low back pain is a major cause of disability leading to absenteeism from work which results in a loss of productivity, with a significant impact on a country's economy (Cohen *et al.,* 2009). It is important to prevent low back pain from becoming chronic in nature, in order to decrease this burden. Typically, low back pain first occurs between 20 to 40 years of age in the majority of the population (Casazza, 2012). Therefore the correct management of acute low back pain may prevent prolonged lifetime episodes.

2.3.2 Classification of low back pain

Low back pain can be classified according to duration of symptoms (Cole, 2002), as seen in Table 2.1.

Table 0.1: A Classification of Low Back Pain

	Duration	Presentation
Acute	Less than two weeks	Usually is resolved when the underlying cause is treated Symptoms may resolve within two weeks or may lead to a chronic condition if left untreated
Subacute	More than two weeks but less than 12 weeks	Despite persistent symptoms, prognosis is still favourable and treatment is directed at maintaining function and preventing disability
Chronic	More than 12 weeks	Pain persists despite normalization after injury and disease and may cause some activity limitations
Acute on Chronic	Isolated episodes of acute pain over time	There is an acute flare up of peripheral tissue pathology due to an underlying chronic pathological entity.

(Atlas and Deyo, 2001; Cole, 2002; Morris, 2006; Balagué *et al.*, 2012; Morrow, 2014)

There are two main types of low back pain. The first type is mechanical in nature and is defined as pain arising from an injury to or malfunctioning of structures of the spine such as the vertebral bodies (VB), joints, ligaments, musculature, dura, spinal cord and nerves (Chien and Bajwa, 2008; Walker, 2012). The second type is non-mechanical low back pain which is attributed to a specific cause such as neoplasia, infection and/or inflammatory arthropathies (Atlas and Deyo, 2001). For the purposes of this study only mechanical low back pain will be discussed.

2.3.3 Pathophysiology of mechanical low back pain

Activities such as a sustained abnormal posture, incorrect ergonomic positioning, excessive bending, twisting and lifting (Ehrlich, 2003; Balague' *et al.,* 2012; Walker, 2012) may injure the anatomical structures of the low back by placing an

unacceptable demand on them which may lead to tissue failure (Morris, 2006). Tissue failure in any of the structures will result in inflammation (Wassung, 2012).

Immediately following tissue damage or any acute injury such as a sprain or strain of the soft tissues of the low back (Cluett, 2014), the body initiates an inflammatory response (Bleakley and Davidson, 2010; Wassung, 2012; Prentice, 2011) to aid in limiting blood loss, removal of metabolites and to allow the development of new capillaries that will transport the materials required for tissue repair (Denegar *et al.,* 2010). The acute inflammatory response is initiated by a variety of chemical mediators such as neutrophils followed shortly by monocytes (Ricciotti and FitzGerald, 2011), eosinophils and macrophages which dominate the initial stages of acute inflammation (Bleakley and Davidson, 2010). These mediators then cause a vascular responses with increased blood flow (Villarreal *et al.,* 2001;Weber, 2009) which results in localised redness and heat with an increase in vascular permeability of local capillaries which causes localised oedema (Wassung, 2012). Oedema may compress localised nerves causing pain (Weber, 2009). This sequence of events is indicative of acute inflammation and the resulting signs are referred to as the cardinal signs of inflammation (Rippey, 2006).

2.3.4 Diagnoses of low back pain

A patient with mechanical low back pain usually presents with pain in the lumbosacral region progressing into the lower limbs, accompanied by muscle spasm and a decrease in range of motion (Levin, 2000). Numbness, tingling or weakness throughout the lower limb may also be present (Dagenais and Haldeman, 2012). It is often characterized by an increase in pain with motion, and a decrease in pain with rest (Karnath, 2003). Diagnosis of acute mechanical low back pain is based on a patient's history (onset, location and duration of signs and symptoms) as well as clinical findings during the physical and orthopaedic examination (Karnath, 2003). If a patient is not responding to a course of conservative therapy or has any red flags or risk factors present, further investigations such as plain radiographs, computed tomography (CT) and magnetic resonance imaging (MRI) may be indicated to confirm a diagnosis (Atlas and Deyo, 2001).

The differential diagnoses for acute mechanical low back pain includes muscular or ligamentous sprain or strain, spondylolisthesis, spondylolisis, spondylysis, disc

herniation, spinal stenosis, fractures, degenerative disease, congenital disorders such as kyphosis and scoliosis, facet joint syndrome, sacro-illiac syndrome, segmental and somatic dysfunction, fibromyalgia, and myofascial pain syndrome (Patel and Ogle, 2000; Atlas and Deyo, 2001;Karnath, 2003).

2.3.5 Management of acute low back pain

Clinicians treating acute mechanical low back pain primarily focus on the reduction of pain, muscle spasm and joint restriction, with the aim of improving functionality and prevent reoccurrence through education (van Tulder *et al.,* 2006; Casazza, 2012 and Dagenais and Haldeman, 2012). Common treatments include non-steroidal anti-inflammatory drugs (NSAIDs) (Patel and Ogle, 2000), muscle relaxants, and opiods to relieve pain (Chou *et al.,* 2007). Many practitioners will utilise more than one treatment intervention to manage acute low back pain (Hills, 2012). The common treatment methods will be discussed to highlight the evidence to support them.

A manual therapy such as massage therapy improves blood circulation, muscle flexibility and aids in the movement of lymph; which in turn assists with pain reduction and improved muscle function (Dagenais and Haldeman, 2012). In a systematic review (n = 10), Furlan *et al.* (2011) identified three clinical trials showing a significant short term reduction in pain and disability associated with low back pain following massage therapy, when compared to placebo or no treatment.

Spinal manipulation (SMT) is another commonly used modality in treating acute low back pain to maximise painless movement, reduce muscle tightness and improve joint mobility (Cohen *et al.,* 2009) by imparting a thrust into a joint to move it beyond its restricted range of motion (Maigne and Vautraves, 2003). A systematic review (n = 39) by Assendelft et al., (2004) found that when compared to placebo or sham therapy, SMT provided greater short term clinical improvements in pain and disability. However, it was also noted that, when compared to other therapies for low back pain such as analgesics, physical therapy, exercise and back schools, SMT did not show greater statistical or clinically significant benefits. These treatments are therapist and clinician dependant making the patient a passive recipient of care.

Patient education is often given as an adjunct to passive care, where the benign nature of acute low back pain is discussed and the patient is reassured that the

condition requires minimal non-invasive interventions to produce significant improvement (Casazza, 2012). Patel and Ogle (2000) noted that a successful treatment involves the patient having an understanding of the condition and their role in preventing re-injury which may be in the form of emphasizing measures to avoid re-occurrence by adopting appropriate postures for sitting, driving and lifting.

In a systematic review investigating the effectiveness of patient education in the treatment of non-specific low back pain, Engers *et al.* (2008) noted that a longer duration (approximately two and a half hours) of verbal patient education was more effective than no intervention and equally effective when compared to non-education interventions such as physical therapy. It was also noted that shorter duration education such as written material was no more effective than no education at all in the management of acute non-specific low back pain.

Exercise is also used in the management of musculoskeletal disorders as it reduces pain and disability associated with low back pain, hastens recovery and prevents re-injury (Long *et al.,* 2004). A variety of different exercises can be used in the management of musculoskeletal pain; these include aerobic, exercise and isometric exercise as well as exercises that promote specific activation and re-education of key muscle groups (Wright and Sulka, 2001). Hayden *et al.* (2005) conducted an extensive meta-analysis of randomised clinical trials assessing the effectiveness of exercise for decreasing pain and disability in adults with acute, sub-acute and chronic low back pain. In acute low back pain, it was noted that there were no significant differences in short term pain relief between exercise and no treatment. There was also insufficient evidence to support or refute effectiveness of exercise in sub-acute low back pain. However, their review found exercise to be as effective as other conservative treatments in improving pain and disability associated with chronic low back pain.

Traditionally, medications have been recommended; however, they are known to cause adverse effects and may only provide temporary relief (Dagenais and Haldeman, 2012). In a systematic review (n = 28) Roelofs *et al.* (2008), noted that the use of NSAIDs in the management of non-specific low back pain was more effective than placebo in providing short-term symptomatic relief for non-specific low back pain. However the use of NSAIDs must be monitored and may not be suitable

for all patients. In terms of muscle relaxants they have been found to be superior to placebo in the management of non-specific low back pain (Van Tulder *et al.,* 2003). Alternatively herbal anti-inflammatory preparations may be recommended as they are less likely to have side effects (Kaur and Guleri, 2013).

In spite of the array of treatment approaches available one of the most common first line treatments is “R.I.C.E.S” (Rogers and Rowland, 2011) which is an acronym for rest, ice, compression, elevation and support (Andrews *et al.,* 2014). It is used to relieve acute pain, limit swelling and protect the injured area (Quinn, 2014). Ice, being the main part of the treatment protocol, is used by clinicians and people as a self-directed home treatment. It is easy to apply and readily available. It decreases blood flow, thus relieving pain and swelling associated with inflammation (Wright and Sluka, 2001; Dagenais and Haldeman, 2012), and has been shown to be effective as a treatment for low back pain, although the evidence is sparse (Dagenais and Haldeman, 2012).

2.4 Cryotherapy

Cryotherapy is defined as the direct application of cold (Cameron, 2012; Beck, 2010) to the skin to decrease both superficial and deep tissue temperatures (Jutte *et al.,* 2001) and has been shown to be an effective modality for managing acute musculoskeletal injuries (Andrew *et al.,* 2014). Practitioners such as chiropractors often utilise cryotherapy (Christensen and Kollasch, 2005) to treat the discomfort associated with acute sprains and strains because it is simple, inexpensive and widely available (Garra *et al.,* 2010).

2.4.1 The mechanism of action

The common principle by which cryotherapy may act is by heat transfer which occurs when the cold modality is warmed by the underlying superficial tissues to which it is applied (Chesterton *et al.,* 2002). This produces a loss of heat from the underlying deeper tissues to the superficial tissues, which eventually cools the area effectively (Merrick *et al.,* 2003). This decrease in tissue temperature brings about physiological mechanisms such as a decrease in metabolic activity and nerve cell conduction (Herrera *et al.,* 2010) along with a decrease in blood flow (Cameron, 2012). This in

turn results in a decrease in the pain and oedema (Enwemeka *et al.,* 2002) associated with most musculoskeletal injuries (Satam *et al.,* 2011).

A variety of cryotherapy techniques exist each with its own thermodynamic properties. Different thermodynamic properties bring about different cooling efficacies (Merrick *et al.,* 2003) which may influence a manual therapist's decision to use a particular modality. For example, cold water immersion has been shown to bring about the greatest decrease in sensory nerve conduction velocity which is possibly due to the large surface area of the body that is in contact with the modality (Herrera *et al.,* 2011). Each method has its own set of practical advantages and disadvantages in terms of use, cost and personal preference (Chesterton *et al.,* 2002) and act along different mechanisms which may be better suited to certain patients.

Three main mechanisms of action have been identified; traditional, where the cold modality will act directly on cutaneous blood flow, nerve cell velocity and pain thresholds (Heinrichs, 2003); excitation of transient receptor potentials (McKemy *et al.,* 2002); and continual tactile stimulation combined with a decrease in tissue temperature (Simons *et al.,* 1999).

2.4.1.1 Traditional methods of cryotherapy and their mechanism of action

This mechanism of action occurs when a cold modality, such as those in Table 2.2, makes direct contact with the skin (Allen, 2006). The decreased tissue temperature results in a "slowing down" of the rate of the chemical reactions which occur during the acute inflammatory response (Bleakley and Davidson, 2010) and in turn reduces the cardinal signs of inflammation (Cameron, 2012).

Table 0.2: Traditional cryotherapy methods and their advantages and disadvantages

Method	Application procedure	Advantages	Disadvantages
Cold pack	A cold pack is usually wrapped in a towel and placed over the affected area for approximately 10 to 15 minutes	Inexpensive, easy to apply; covers a moderate to large area and requires a low level of skill by the user.	Requires refrigeration and requires a barrier, such as a towel, between the cold pack and the skin to prevent burns. The patient may not tolerate the weight of the cold pack and the cold pack may not maintain contact with small or contoured areas.
Ice massage	An ice massage is performed by making use of an ice cube, which is massaged over the affected area. Some techniques make use of a disposable cup filled with water and then placed in a freezer. These ice cups provide a mould and a handle for the therapist to apply the ice massage without freezing their hand.	Inexpensive and is easily applied over smaller irregular areas. The treatment area can be observed during the application of the ice massage.	May be time consuming to apply over larger areas, the ice quickly melts, making the application messy so it can only be applied for a short period of time. This method of cryotherapy also requires refrigeration
Cryopressure garments	Cryopressure garments utilise cold fluid and air that is circulated through a sleeve that is wrapped around the patient's limb. The temperature is controlled by adjusting the controls of the unit.	Combines cryotherapy with compression and can be applied for extended periods of time as the temperature is able to be controlled by the compression unit.	Expensive and a bulky piece of equipment. Unable to be applied on the trunk or the digits and is used for the extremities only.

(Chesterton *et al*., 2002; Airaksinen *et al.,* 2003; Beck, 2010; Cameron, 2012)

Cryotherapy reduces the heat associated with inflammation by decreasing the temperature of the area to which the cold modality is applied (Chesterton *et al.,* 2002). The decreased tissue temperature causes vasoconstriction which decreases cutaneous blood flow and increases blood viscosity (Nadler *et al.,* 2004; Heinrichs, 2003). This may take place through both direct and indirect mechanisms.

The direct application of cold to an area of the body stimulates the smooth muscle in the blood vessel walls to contract, thus constricting blood flow to the area (Naish *et al.,* 2009). Indirectly, cooling of tissue can bring about vasoconstriction through a variety of mechanisms such as a decrease in the production and release of vasodilator mediators, such as histamine and prostaglandins, resulting in a decrease in vasodilation. In addition, reflex activation of the sympathetic adrenergic neurons also takes place following the application of cold; resulting in cutaneous

vasoconstriction in the area that is being cooled and in the area distant to the site of cold application, although this distant vasoconstriction may be less pronounced (Cameron, 2012). This coupled with a decrease in capillary permeability hinders the movement of fluid from the capillaries to the interstial space, thereby controlling bleeding and fluid loss following a tissue trauma (Davy, 2012). These effects reduce the redness and oedema associated with inflammation, alleviating pain as there is no longer compression on the nerves or other pain sensitive structures in the area (Cameron, 2012).

A reduction in nerve cell velocity (NCV) and an increase in pain threshold (Saeki, 2002) may also take place. NCV refers to the speed at which a nerve conducts information to the central nervous system (Davy, 2012). A temperature decrease of a nerve leads to a reduction in the NCV of that nerve in direct relation to the duration and degree of the temperature change (Algarfly and George, 2007). Cold can decrease the NCV of both sensory and motor nerves and has been shown to have the greatest effect on the conduction velocity of smaller, myelinated nerve fibres such as the A-delta fibres (Cameron, 2012). These pain transmitting fibres are known as nociceptors (Purves *et al.,* 2001). A decrease in NCV of the nociceptors will produce a reduction in painful stimuli that reaches the central nervous system and as a consequence, a decrease in pain (Davy, 2012).

An increase in the pain threshold (PT) and a decrease in the sensation of pain are noted after the application of cryotherapy modalities such as ice (Cameron, 2012). Algafly and George (2007) conducted a control based clinical trial (n = 23) and showed that the PT was increased by 89 percent after the skin temperature was decreased to 10 °C. This is most likely due cold that acts as a counter irritant via the gate control mechanism and leads to a decrease in muscle spasm and post injury oedema (Davy, 2012).

The gate control mechanism proposed by Melzack and Wall (1965) states that the stimulation of large-diameter myelinated afferent fibers (e.g Aβ fibres) by non-noxious or non-painful stimuli inhibits second-order neurons in the dorsal horn. This prevents pain impulses carried by small-diameter unmyelinated fibers such as Aδ and C fibres (Reddi *et al.,* 2013) from reaching higher brain centres, thereby inhibiting perception of pain at spinal cord level (Wright and Sluka, 2001).

Stimulation of the cutaneous cold receptors will provide sufficient sensory input to fully or partially block the transmission of pain stimuli along the spinal cord to the cerebral cortex (Cameron, 2012). This in turn will increase the PT, decrease pain sensations and reduce muscle spasm by interrupting the pain-spasm-pain cycle, as illustrated in Figure 2.2.

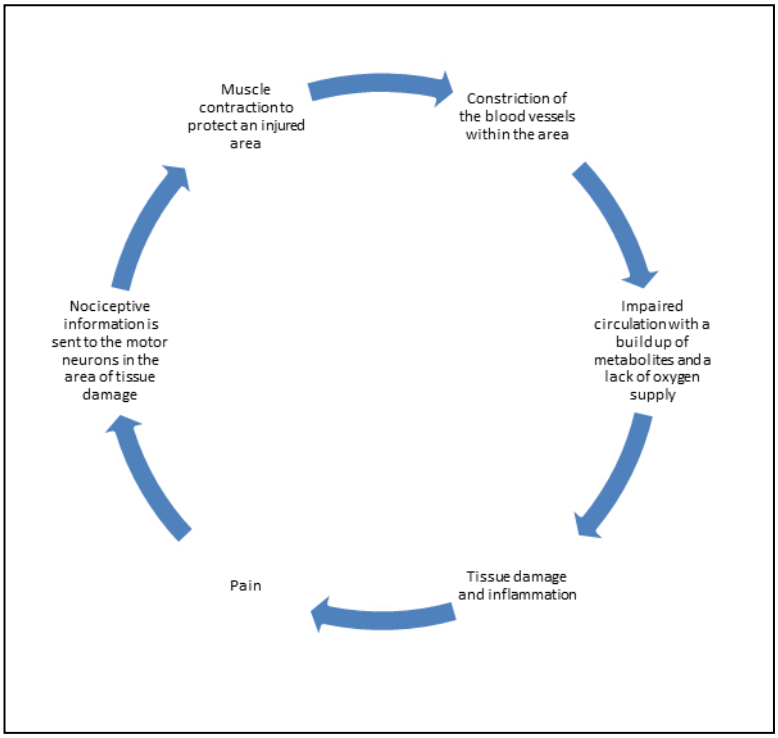


Figure 0.2: The Pain-Spasm-Pain Cycle
(Richards, 2011; Vignoli, 2011)

This cycle shows that even the slightest amount of tissue damage will result in nociceptor information being sent to the motor neurons in the area of the tissue damage resulting in muscle contraction in order to protect the injured tissue. If this muscle contraction continues, it may result in local ischaemia as the blood vessels in the area are constricted; this constriction and the lack of oxygen rich blood in the area can lead to pain (Richards, 2011), thus perpetuating the cycle as the motor neuron will then be re-stimulated (Vignoli, 2011).

2.4.1.2 Cryotherapy methods that utilise the excitation of the transient receptor potential ion channels and their mechanism of action

Another proposed mechanism of action of cryotherapy may be the activation of transient receptor potential (TRP) ion channels following the application of compounds such as menthol (Patel *et al.,* 2007). TRP ion channels are a distinct

subset of sensory neurons (MacPherson *et al.,* 2006) which sense changes in temperature (Peier *et al.,* 2002).

Recently, a receptor for cold has been identified and named the transient receptor potential melastatin 8 (TRPM8) (Bharate and Bharate, 2012). This receptor is part of the transient receptor potential family of excitory ion channels that is hypothesized to act as a transducer of cold stimuli in the somatosensory system (McKemy *et al.,* 2002). TRPM8 is an ion channel that modifies the concentration of sodium and potassium ions that are crossing the membranes of nerve cells (Peier *et al.,* 2002). The concentration of these ions controls the release of glutamate (Tsuzuki *et al.,* 2004; Bharate and Bharate, 2012), an important neurotransmitter (Purves *et al.,* 2001) which is able to inhibit nociceptive information to the central nervous system (Fundytus, 2001). Glutamate also plays a role in gene transcription, muscle contraction and cellular proliferation (Bootman *et al.,* 2001). Thus, the activation of TRPM8 by cooling compounds such as menthol is able to assist the blockage of nociceptive information to the brain (Bharate and Bharate, 2012). Two of the cooling gels used for the treatment of low back pain contain menthol as an ingredient (Topp *et al.,* 2011).

Menthol is a naturally occurring compound which gives plants of the *Mentha* species its characteristic ‘minty’ taste and smell (Eccles, 1994; Galeotti *et al.,* 2002). When applied to the skin in small doses it produces a pleasant cooling sensation (Bharate and Bharate, 2012), possibly due to the constriction of the blood vessels in the skin which decreases the temperature locally (Wasner *et al.,* 2004). In a comparative study (n = 17), comparing a menthol gel (3.5 percent menthol) to ice on the blood flow of the radial artery, it was noted that the menthol gel decreased blood flow in the radial artery after 5 minutes and ice only produced the same effect after 20 minutes (Topp *et al.,* 2011). This may indicate that menthol acts faster than ice to decrease tissue temperature and bring about therapeutic effects.

Apart from menthol’s effects on TRMP8 channels and calcium influx, it may also work to enhance the penetration of drugs when combined in solutions such as cooling gels, as it has the ability to penetrate the epidermis and allows for greater accessibility to the underlying tissues (MacPherson *et al*., 2006).

Cooling gels are applied to and gently rubbed into the skin of the affected area, which ensures maximal transmission of the gel (Kaur and Guleri, 2013). These gels are convenient because they can be carried by the patient as they do not require refrigeration to stay cold (Airaksinen *et al.,* 2003). They are fast-acting on the applied area; deliver the treatment intervention to the site of application to enhance local effects and minimize systemic effects (Kaur and Guleri, 2013). Another advantage is that even after the sensation of cold has ceased, the active ingredients present within the gel can still be absorbed and bring about a therapeutic effect. However, the decrease in blood flow may be short-lasting (Topp *et al.,* 2011); the cooling gels may irritate the user's skin or may cause an allergic reaction (Moody, 2010).

2.4.1.3 Cryotherapy methods that utilise continual tactile stimulation and their mechanism of action

Vapocoolant sprays produce both a direct cooling of the tissues by evaporation as well as tactile stimulation of the area being treated and are often used on the trigger points located within a muscle (Simons *et al.,* 1999). The continuous stream of spray causes a bombardment of impulses to the spinal cord which could inhibit locally generated pain (Cameron, 2012). Vapocoolant sprays have also been hypothesized to be effective in acting as a counter irritant to cutaneous afferents which would then decreases motor neuron activity (Starkey, 2013). These neural mechanisms help the subsequent muscle to relax and can often be followed with stretching of that muscle, a technique known as "spray and stretch" (Simons *et al.,* 1999). However, the therapeutic effects may be temporary and may act superficially. Vapocoolant sprays contain Fluori-Methane, which may be a possible narcotic or have a general anaesthetic effect if it is inhaled by the patient (Beck, 2010).

2.4.2 Menthol cooling gels with additional additives

Menthol has an added benefit in that it enhances the penetration of ingredients such as topical anaesthetics (Liu *et al.,* 2005), therefore making it beneficial to include other agents in menthol gel formulations. Menthol reacts with the intact skin and may disturb the barriers to penetration of exogenous materials, making the skin more permeable and thus the ingredients combined with menthol are able to be delivered transdermally (Karande and Mitragatri, 2009). The sensation of cooling to the skin brought about by cooling gels lasts several minutes (Liu *et al.,* 2005). Following this

the active ingredients combined in the gel are absorbed and can further facilitate healing. Once menthol is administered topically, it is absorbed into the systemic circulation (Margetts and Sawyer, 2007), metabolized to menthol glucuronide in the liver and later excreted in the urine (Andersen *et al.,* 2013). The half-life of menthol that is applied transdermally is 96 minutes (Martin *et al.,* 2004).

Additional ingredients are often added to aid healing during the inflammatory phase, and may make them more appealing to people suffering with musculoskeletal disorders such as low back and neck pain. The cooling gel utilized in this study, consists of 0.76 percent menthol however it also contains anti-inflammatory herbs, which make up less than 0.5 percent of the total formula (referred to as H8000 for proprietary reasons). The herbal extract (H8000) is a combination of 248 different chemical compounds and organic herbal extracts which work together to produce anti-inflammatory effects. According to Gerber (2013) this gel is popular amongst people who suffer with musculoskeletal pain as a topical cooling gel and it is readily available in pharmacies across South Africa without the need for a prescription. There have also been no reported adverse reactions following its use (Gerber, 2013).

The two main ingredients of H8000 are Arnica and Echinacea (Gerber, 2013). Arnica is a popularly utilized substance that is beneficial in treating bruises, sprains, muscle aches and other conditions caused by trauma and overexertion (Wagner *et al.,* 2004). The active components of arnica are compounds known as sesquiterpenoid lactones (SLs) which are known to produce anti-inflammatory effects (Wagner *et al.,* 2004) and analgesia. The SLs consist of esters such as helenalin, dihydrohelenalin and chamissonolid (Anselmo, 2003) which act on various cellular processes such as oxidative phosphorylation, platelet aggregation, histamine and serotonin release (Lyss *et al.,* 1998). Helenalin, in particular, has been shown to inhibit DNA binding activity of the transcription factor, NF-KB (Lyss *et al.,* 1998). NF-KB is involved in the expression of cytokines, such as interleukin-1 and Tumour Necrosis Factor (TFN), chemokines and adhesion molecules (Wagner *et al.,* 2004; Lawrence, 2009) which are all rapidly released following tissue injury and infection (Lawrence, 2009) leading to inflammation.

The combination of herbal extracts in H8000 and Echinacea produce a synergistic effect (Gerber, 2013). Echinacea relieves pain, brings about antioxidant and immunostimulatory effects and reduces inflammation (Ernst, 2002). Active ingredients in Echinacea include polysaccharides, glycoproteins, alkamides, flavinoids, phenolic acid derivatives and lipophilic compounds (Rininiger *et al.,* 2000; Ernst, 2002; Kliger, 2003 and Kumar and Ramaiah, 2011).

The anti-oxidant effects are brought about by the phenolic acid derivatives which enhance free radical scavenging activities and promote anti-hyaluronidase activity (Kumar and Ramaiah, 2011). Hyaluronidase is an enzyme used by a number of bacteria to penetrate tissues (Rininiger *et al.,* 2000).Inhibition of the hyaluronidase by these derivatives helps to maintain cell integrity (Gerber, 2013). The immunostimulatory effect of Echinacea are a result of polysaccharides found in the plant which stimulate the phagocytic activity of macrophages and neutrophils (Kumar and Ramaiah, 2011) which in turn allow for future recognition of the engulfed cell and thus enhance cell mediated immunity (Peiser and Gordon, 2009).

The inhibition of inflammatory mediators such as tumour necrosis factor alpha (TNFα) and nitric oxide (NO) and prostaglandin E2 (Kumar and Ramaiah, 2011),by echinacoside, which is found in Echinacea, causes a reduction in inflammation (Speroni *et al.,* 2002). In this regard, an animal study (n = 15) showed that the oedema and redness associated with acute inflammation were markedly reduced at 24 hours after the topical application of Echinacea (Speroni *et al.,* 2002).

Table 0.3: Clinical Research Utilising Menthol Based Cooling Gels Combined with Herbal Ingredients

Reference	Sample Size	Study Design	Intervention	Outcome
Zhang *et al., (*2008)	n = 34	Randomized controlled study	Biofreeze® in conjunction with lumbar spine manipulation versus lumbar spine manipulation (SMT) alone in the treatment acute low back pain	Combination group showed significant ($p < 0.05$) reductions in pain compared to lumbar SMT only
Bishop *et al.,* (2009)	n= 51	Randomized clinical trial	Biofreeze® compared to ice in acute non-complicated neck pain	Biofreeze® decreased pain levels twice as much as ice ($p < 0.001$)
Harper, (2010)	n=48	Double blinded randomised controlled clinical trial	Compared an ice pack, a menthol based gel, a menthol based gel with herbal extracts (the gel used in this study) and a placebo gel in grade 1 and 2 ankle inversion sprains	All interventions improved pain, disability, pressure pain threshold and swelling with the active interventions showing greater improvements ($p<0.001$) than placebo
Satam *et al.,* (2011)	n=45	Open clinical trial	The clinical efficacy and long term safety of a herbal gel in the management of pain and inflammation associated with chronic musculoskeletal disorders	The herbal cooling gel improved pain scores, joint tenderness, joint swelling, joint mobility restrictions and early morning stiffness. No statistical values were provided but it was reported that there was a significant reduction in pain, tenderness, swelling, joint immobility and early morning stiffness.

Both Bishop *et al.* (2009) and Zhang *et al.* (2008) utilised the menthol herbal gel Biofreeze® and found it to be beneficial in the treatment of neck and low back pain.

Although the pathophysiology of injury in these two areas may be similar, the depth of the structures differs. Biofreeze® consists of 3.5% menthol as the active ingredient along with other inactive ingredients (Drugs.com, 2014). This gel is currently not commercially available in South Africa. The participants in Bishop *et al.,*(2009) study were given both ice and Biofreeze® concurrently, thus it would have been difficult for the participants to distinguish between the two modalities and comment on the reduction in pain. In addition, the study used only subjective measurement tools (Visual analogue scale) and blinding would have not been possible, which would have affected the outcome of the results. The clinical trial conducted by Zhang *et al.,* (2008) was a single-blinded clinical trial in which the researcher was blinded from which treatment the participants were receiving. This would have eliminated any bias from the trial but as different chiropractors were used to administer the spinal manipulation this could have introduced variability and possibly influenced the results.

The gel used by Satam *et al.* (2011) consisted of methyl salicylate, Cedrus deodara,, Boswellia serrata, Eucalyptus oil, as well as menthol, camphor and capsicum oleoresin. The quantities of each were not given. Although they found a clinically significant reduction in terms of relieve from pain, swelling and tenderness, they included participants with a variety of conditions from inflammatory arthropathies to spondylosis and the design utilised was weak as there was no control group, and the natural history of the conditions were not taken into account. However the results warrant further investigation with more stringent research designs.

Harper (2010) utilised a locally produced menthol cooling gel with anti-inflammatory herbs (the same one used in this study) and found that it resulted in a similar effect as an ice pack and a menthol only gel in the treatment of grade one and two ankle sprains. Menthol and traditional ice packs work on a different mechanism of action as described previously, but from this study appeared to have a similar impact on pain, disability and pressure pain thresholds. The lack of increased efficacy of the menthol cooling gel with anti-inflammatory herbs may indicate that the anti-inflammatory effect of the herbs is not powerful enough to improve outcomes, over those as a result of menthol alone. This study had a small number of participants in each group (n = 12); with a larger sample size the results may have been different. In

addition there is limited research on this gel with which to compare these results, and comparison to other gels such as Biofreeze® is difficult as the ingredients and their concentrations differ. Another consideration is the depth of the structures being treated; the ankle joint is a relatively superficial area as compared to deep tissue such as the structures of the low back in which its efficacy has not yet been determined.

Presently, topical analgesic ointments are un-regulated in South Arica but the regulatory laws are presently being re-assessed. As a result, many products are available to the public that may not have been through careful scientific testing. By scientifically investigating these products, their efficacy and safety of use can be determined and enhanced if need be (Johnston, 2012). This will benefit the user and the clinician who is recommending or themselves utilising these gels. The novel gel in this study has been shown to be safe and effective in reducing pain and swelling of grade one and two ankle sprains, however it has not been investigated in other musculoskeletal conditions, thus an investigation into the efficacy and safety of this novel gel in other conditions should be under taken.

2.4.3 Factors affecting the successful application of menthol cooling gels

A number of factors have been recognised as affecting the successful application of cooling modalities. However, factors like the ability of the ice pack to conform to the area of injury, the duration of application time and the ability of the cryotherapy technique to undergo a phase change are not relative to cooling gel applications. An individual's body fat percentage may influence the efficacy of certain cooling modalities as people with a lower body fat percentage may exchange heat faster than those with a higher percentage body fat (Heinrichs, 2004). Body fat percentage is related to the body composition of an individual, when assessing body composition, a measurement of waist circumference or body mass index (BMI) can be done (Esmat, 2012). This is measured by calculating a ratio, using an individual's weight and height, as seen in Table 2.5.

Table 0.4: Relationship between BMI and Nutritional Status

BMI (kg/m²)	Nutritional Status
<18.5	Underweight
18.5 – 24.9	Normal
25-29.9	Overweight
> 30	Obese
>40	Morbidly obese

(Dalton *et al.,* 2003; Celan and Turk, 2005; Tobin *et al*., 2009)

However, cooling gels are applied to the skin and absorbed through the capillaries in the dermis (Tadicherla and Berman, 2006), the layer before the subcutaneous fat layer (Kolarsick *et al.,* 2011). From these capillaries, the ingredients in the gel are absorbed into the systemic circulation via the cutaneous blood vessels (Margetts and Sawyer, 2007). Once the active ingredients have been absorbed into systemic circulation, they are able to reach the target sites where they will bring about their effect (Sawynok, 2003). Thus the amount of subcutaneous fat does not play a role in the efficacy of absorption of the cooling gel as these gels are absorbed superficial to this layer.

A factor to consider is that cooling gels should only be used in individuals who have intact skin (Derman and Schwellnus, 2010), have no skin conditions such as eczema in the area of application and are not allergic to any of the contained ingredients. Other than this they are considered relatively safe (Johnston, 2012).

2.4.4 Methods of assessing the effect of cryotherapy modalities

In order to assess the effect of cryotherapy modalities, the condition being treated can be observed through subjective and objective measurements or for physiological changes. Only the commonly used clinical measures will be discussed below:

2.4.4.1 Measures of pain

Pain is a subjective measurement and is measured using a pain scale. Two common scales are the Visual Analog Scale (VAS) and the Numerical Pain Rating Scale (NPRS). The VAS involves a ten centimetre line with “no pain” marked at one end and “worst pain ever” marked at the other end (Johnson, 2005 and Bleakley *et al.,* 2006). Even though this test possesses a high level of reliability when used repeatedly on the same patient (Bleakley *et al.,* 2006), it was found by Bijur *et al.,*

(2001), that some patients had difficulty in translating the subjective experience of pain into a distance measured on a quantitative scale.

The NPRS uses whole numbers (Johnson, 2005) in which patients rate their current pain intensity from zero “no pain” to ten “worst pain possible” (Krebs *et al.,* 2007). Pain is a multi-dimensional experience and the NPRS may fail to identify the patient with pain related to functional limitations, worry, illness or other factors (Krebs *et al.,* 2007). The NPRS is short, easy to administer and its validity as a measure of pain intensity has been validated in populations with known pain. Krebs *et al.,* (2007) found that the area under the ROC curve for pain screening was 0.76 indicating fair accuracy when compared with the primary reference standard. The minimal clinically significant change when using a numerical pain rating has been shown to be two, which is equivalent to a percentage of 20% for low back pain (Childs *et al.,* 2005 and Ostelo and de Vet, 2005). NPRS is often chosen as the pain measurement tool of choice because it is a simple and robust measurement method (Ostelo and de Vet, 2005). The established cut off points for patients using the NPRS are a rating of one to four, indicates mild pain; four to six indicates moderate pain and seven to ten indicates severe pain (Jones *et al.,* 2007).

2.4.4.2 Measures of disability

Disability is a subjective measurement tool and assesses a patient’s response to treatment (Davidson and Keating, 2002). In patients with acute low back pain that is mild to moderate in nature the Roland Morris Disability Questionnaire (RMDQ) is recommended (Davies and Nitz, 2009). It is a self-administered questionnaire made up of 24 statements reflecting a variety of daily living activities and a patient’s perceived level of disability when performing these activities. Each item is scored one if the patient finds it applicable to them or zero if not, thus the RMDQ is scored out of 24 (Monticone *et al.,* 2012). It is short and simple to complete and the statements are readily understood by most participants (Roland and Fairbank, 2000). The clinical significant change of the RMDI is 3.5 points, which is 14.6% when converted to a percentage (Ostelo and de Vet, 2005). The cut off points for the RMDQ are zero to eight is mild disability, nine to 15 is moderate disability and 16 to 24 is considered to be severe disability (Bissolotti *et al.,* 2013).

2.4.4.3 Measures of pressure-pain threshold

Measuring pressure-pain threshold (PPT) allows the clinician or researcher to objectively measure pain associated with trigger points and to evaluate the effectiveness of treatments which attempt to alleviate pain (Pottera *et al.,* 2006). An algometer is commonly utilised for this purpose. It is a hand held device used to measure the amount of constant pressure or force needed to produce pain at a particular point (Nussbaum and Downes, 1998; Kinser *et al.,* 2009). Using only one examiner it has been shown to have good repeatability (Ylinen *et al,* 2007); however, it has been associated with some difficulty when assessing the rate of pressure exerted by the examiner and the examiner's response time (Antonaci *et al.,* 1998). The minimal clinical significant change is 1.5kg/cm^2 (Chesterton *et al.,* 2007).

2.4.4.4 Measures of blood flow

Some studies (Fiscus *et al.,* 2005; Holwera *et al.,* 2013) have assessed the effect of cryotherapy methods on blood flow using strain gauge plethysmography. This consists of a four wire limb gauge consisting of a transducer with a silicone rubber tube filled with mercury or an indium-gallidum alloy (Lanzer and Topol, 2002). This is placed around the middle of a muscle of a limb and cuffs are placed above and below the gauge (Fiscus *et al.,* 2005). As the blood flow inside an artery increases, the strain gauge is stretched (Lanzer and Topol, 2002). Strain gauge plethysmography is non-invasive but it may be difficult to calibrate, is expensive and is sensitive to changes in temperature and limb positioning (Lanzer and Topol, 2002).

Another common method is Doppler ultrasound, a non-invasive, risk free and pain free (Sheps, 2014) measuring tool which utilises the propagation of ultrasonic waves in tissues to asses blood flow through an artery (Jayanthy *et al.,* 2011). This has been shown to possess good to moderate inter-observer reliability but poor repeatability and is operator-dependent (Dasgupta and Patil, 2012).

2.5 The placebo effect

A placebo is a "sham" or false treatment which can be either a drug or substance which has no active ingredient (Stewart-Williams and Podd, 2004), a surgery or any other "pretend" procedure that mimics the active treatment (Friedman and Dubinsky,

2008). Placebo interventions are used in research to determine if a treatment is effective for a specific condition and the changes noted in the group receiving the active treatment are compared to the changes noted in the placebo group (Friedman and Dubinsky, 2008). A placebo should preferably be identical in look, smell and taste to the active treatment (Rajagopal, 2006).

A self-administered survey (n = 183) investigating the knowledge and attitudes of local clinicians and researchers regarding the use of placebo in clinical trials, concluded that 60 percent of those surveyed would use placebo in a clinical trial (Lau *et al.,* 2003). In some instances, participants in the placebo group of an RCT may improve; this is due to the placebo effect (Lau *et al.,* 2003).

2.5.1 Mechanism of action

The placebo effect is a psychobiological phenomenon (Benedetti *et al.,* 2005 and Meissner *et al.,* 2010) which may be attributed to expectation of clinical improvement, pavlovian conditioning (Benedetti *et al.,* 2005), empathy, social learning, emotion and motivation, spirituality and healing rituals (Meissner *et al.,* 2010). It has been noted that the endogenous opioid system in the brain may be involved in placebo and thus the same pathways that are involved in placebo are also involved in pain reducing mechanisms (Meissner *et al.,* 2010). Petrovic *et al.* (2002) noted in a clinical trial (n = 9), that similar brain regions were affected by placebo or by treatment with opioid analgesics when treating pain. Although this study had a small sample size, the authors were able to show statistically significant results ($p = 0.005$).

Zubieta *et al. (*2005) found that the expectation of pain relief activates opioid receptor signalling in the human brain. Expectation and classical conditioning may also explain the psychological mediation of the placebo effect (Meissner *et al.,* 2010). Expectation or expectancy is defined as an individual's belief about forthcoming events (Rutherford *et al.,* 2010); a placebo may bring about a particular effect that the recipient expects it to, and thus it is the expectation itself which is able to bring about the placebo effect (Stewart-Williams and Podd, 2004). If a placebo intervention is expected to produce analgesia, recipients have been shown to have a reduction is self-defeating thoughts and an increase in coping cognition and thus the perception of pain is decreased (Stewart-Williams and Podd, 2004).

A clinic trial (Benedetti *et al.,* 1999) suggested that the expectation of pain relief in a particular area of the body will cause a reduction in pain in those particular areas only. Benedetti *et al.,* (1999) conducted a double-blinded randomized clinical trial (n=173) in which neither the researcher nor the participant was informed as to which analgesic drug was being administered. This would have eliminated any bias and the large sample size would have ensured statistically significant ($p < 0.001$) results.

Researchers have noted that classical conditioning occurs when a recipient improves after being treated with a particular medication or therapy and the recipient is then conditioned to expect an improvement by a subsequent medication or therapy, even a placebo (Rajagopal, 2006; Meissner *et al.,* 2010).

It is often questioned whether it is ethically correct to give a placebo treatment to a patient with a disease or a disorder and then not make the patient aware that they are receiving a placebo treatment. RCTs are carefully monitored to be certain that the participants who are receiving the placebo treatment are not subjected to any serious or irreversible harm (Lau *et al.,* 2003) and it has become the norm in RCTs to allow all participants to receive treatment on completion of the study (Friedman and Dubinsky, 2008).

In the end, all participants benefit from RCTs that are conducted using a placebo so that the true effectiveness of the treatment can be fully understood (Friedman and Dubinsky, 2008).

2.6 Conclusion

From the review of available the literature, it can be concluded that the inflammation associated with acute non-specific low back pain may respond well to modalities such as cryotherapy. Cooling gels are a novel form of cryotherapy that is favourable amongst individuals as it is easy to administer, relatively inexpensive and convenient to transport as it does not require refrigeration. Cooling gels are able to be combined with other ingredients such as anti-inflammatory herbs that may enhance their effect, however, the scientific evidence to support their use is lacking.

CHAPTER THREE: MATERIALS AND METHODS

3.1 Study design

This study was designed as a double blinded placebo controlled clinical trial. This design was chosen as clinical trials are considered to be the “gold standard” in establishing the efficacy of treatment interventions (Meissner *et al.,* 2011) and it was randomized to ensure that the control and intervention subjects were similar in all known and unknown attributes (Nallamothu *et al.,* 2008) which might have influenced the study outcome.

Double blinding is used in RCTs to ensure the responses to an intervention are not affected by knowledge of group allocation (Shulz and Grimes, 2002). In cases where neither the researcher nor the participant is aware of which treatment group he or she has been allocated to, it limits bias (Bhattacharya, 2006). The study received ethical clearance from the Institutional Research Ethics Committee of the Durban University of Technology (Ethical Clearance Number 006/114; Appendix C).

3.2 Participant recruitment

Participants were recruited through advertisements (Appendix D) in the form of posters which were placed at the Durban University of Technology campuses of Steve Biko, Ritson Road and ML Sultan, and at the Howard and Westville campuses of the University of KwaZulu Natal. In addition the adverts were placed at shopping malls and various sports clubs throughout the greater eThekwini municipality. Permission was obtained prior to placing advertisements (Appendix E). Word of mouth was also used to recruit participants.

3.3 Sampling

3.3.1 Sample size

A sample size of 60 participants was required for this study. A power analysis conducted using G-Power and for the statistical test, analysis of variance with repeated measures, within-between group interactions, with a medium effect size

(0.4), an alpha of 0.05 and a power at 80%, showed that a minimum of 18 participants were required per group.

3.3.2 Sample strategy and allocation

Participants were randomly assigned into one of three treatment groups by using a randomized allocation chart. A statistician generated an unpredictable random sequence of group allocation for 70 participants, in order to account for any potential dropouts from the study.

Participants were allocated to one of three groups:

Group One: Menthol based cooling gel containing anti-inflammatory herbs

Group Two: Menthol based cooling gel

Group Three: Placebo gel which contained no anti-inflammatory herbs or menthol

3.3.3 Participant characteristics

People responding to the advertisements contacted the researcher telephonically, after which they were screened using the following questions:

1. How old are you?
2. How long has your low back pain been present?
3. Do you have any open wounds, healing burns or infectious skin diseases on your lower back area?
4. Have you had any surgery to your lower back area?
5. Are you cold intolerant or feel uncomfortable in a cold environment?

Potential participants had to be between the ages of 18 and 40 years, with low back pain that had been present for no longer than one week to indicate that the condition was still in the acute phase (Coste, 1994). The potential participant had to have no open or unhealed lesions and infectious skin disorders on the low back area. If the potential participants had any surgery to the low back, they were excluded (Kirkaldy-Willis and Burton 1992). Potential participants presenting with cold hypersensitivity or circulation impairments were excluded from the study as this is a contraindication to cryotherapy (Morgan, 2012; Knight, 1985). The information gathered in the telephonic interview remained confidential regardless of whether the participant was included or excluded from the study. If the participant did not meet the screening

criteria for inclusion, they were thanked for their time and appropriately referred if necessary.

If the respondent met the criteria, they were invited to attend a consultation at the Chiropractic Day Clinic (CDC) located at the Durban University of Technology, where permission to conduct the study was obtained from the clinic director (Appendix F).

On arrival for their consultation each participant received a verbal explanation about the study and was given a letter of information and informed consent (Appendix G) detailing the research and what would be expected of them. The participants were informed that they were free to withdraw at any time and were given an opportunity to ask questions about the study. On agreeing to participate, they were required to sign the letter of information and informed consent; they then underwent a case history (Appendix H), physical examination (Appendix I) and a lumbar spine examination (Appendix J) to determine their eligibility to join the study according to inclusion and exclusion criteria as listed below.

Participant inclusion criteria:

1. Participants were only accepted into the study once they had given their informed consent in writing.
2. All participants had to be at least 18 years of age to ensure that the patient was skeletally mature and not older than 40 years of age to decrease the chance of sacro-illiac or spinal degeneration (Kirkaldy and Bernard, 1999).
3. The participant had to have low back pain which had been present for no longer than one week.
4. Participants had to be diagnosed by the researcher as having mechanical low back pain according to these criteria:
    - Pain had to be located posteriorly in the area between the lower rib margin and the proximal thighs.
    - Pain may have radiated into the upper thigh and buttocks area.
    - No neurological deficits and no nerve root tension signs as indicated by a negative straight leg raise test.
    - Some of the following orthopaedic tests may have been positive; sacro-illiac (SI) compression test, Gaenslans test, Patrick FABER and Kemp’s Test.

5. A numerical pain rating of three to six, to ensure participants had moderate pain allowing for a homogenous sample.

Participant exclusion criteria:

1. Participants who presented with contraindications to cryotherapy such as:
    - Hypersensitivity to the cold.
    - Emotional reaction to the cold.
    - Cryoglobulinemia.
    - History of pyoderma gangrenosum, skin diseases, cold hemoglobinuria, cardiac disease, Raynaud's Disease.
    - Impaired blood circulation.
    - Malignancy in the area.
2. Participants who presented with the following contraindications to the anti-inflammatory herbs used in the cooling gel:
    - Pregnant or lactating females - the use of arnica during pregnancy is not recommended (Jellin *et al.,* 2002).
    - Allergies to plants in the daisy family such as ragwood, marigold and chrysanthemums as these plants belong to the same plant family as Echinacea (Kliger, 2003).
3. Participants who had open wounds, hypersensitivity to menthol, burns or were using anticoagulant medication (Heparin, Warfarin and Aspirin) were excluded.
4. If it was suspected that a participant had a pathological process such as infection, inflammatory spondyloarthropathies and malignancy (Morris, 2006) causing their LBP they were excluded.

3.4 Measurement tools

The effect of the independent variables (menthol gel with anti-inflammatory herbs, menthol gel and placebo gel) will be recorded by utilising the following dependent variables:

3.4.1 Objective measurements

3.4.1.1 Pressure-pain threshold

An algometer was utilised to determine the amount of pressure required to cause pain, called the pressure-pain threshold (Nussbaum and Downes, 1998; Ylinen, 2007). The algometer used in this study was a Wagner Force Dial ™ FDK/FDN Series Push Pull Force Gauge, and is commercially available through Wagner Instruments P.O Box 127 Greenwich, CT 06836. The handheld device was a force gauge, ranging from zero to 10kg which makes use of a maximum hold function; it is fitted with a disc shaped rubber tip with a surface area of 1 cm^2. The device was placed perpendicular to the skin and pressure was applied steadily at a constant rate. The algometer registered the force applied to the tissues in kilograms per square centimetre (kg/cm^2). The following procedure was utilised in this study for this measurement tool:

1. The same algometer was used for the duration of the study for all the participants. The dial was set to zero and the procedure was explained to the participants.
2. The researcher identified active trigger points within the muscles of the low back, using palpation and verbalisation by the participant to indicate that a particular area was tender which was then marked with a henna pen, while the participant was positioned prone.
3. The rounded application rubber tip of the algometer was placed over the henna marked area at a 90 degree angle to the skin. Pressure was applied slowly and gradually until the participant indicated that pain was felt and the pressure gauge was stopped at this point.
4. This reading was then recorded in Kg/cm^2.

The algometer has been found to be reliable and valid in terms of intra-examiner reliability (r = 0.990) of pressure rate application (Kinser *et al.,* 2009), and intra-examiner reliability when taking measurements on subsequent days (ICC of 0.87 between visit one and two, and an ICC of 0.95 between visits two and three) (Pottera *et al.,* 2006). In order to assess clinically significant changes a difference of 1.5 kg/cm^2 (Chesterton *et al.,* 2007).

3.4.2 Subjective measurements

3.4.2.1 Pain rating

Pain rating was determined by using the numerical pain rating scale (NPRS) in order to establish pain severity (Appendix L). Participants were asked to rate their pain severity by indicating on a scale from zero (no pain) to 10 (the worst pain imaginable), the number which most accurately reflected their pain (Johnson, 2005; Childs *et al.,* 2005).

The test-retest reliability of the NRS has been shown to vary from 0.67 to 0.96 indicating high to moderate reliability (Kahl and Cleland, 2005) and it has been shown to be valid as a measurement of pain intensity (Ferreira-Valente et *al.,* 2011). The minimal change needed for clinical significance was found to be a change of three points (Finch *et al.,* 2002; Kahl and Cleland, 2005). In more recent literature, Childs *et al.* (2005) (n = 131) found that that in a LBP population a two point change indicated clinical significance. As this study measured the change in NPRS regarding LBP, a two point change was considered clinically significant.

3.4.2.2 Disability from low back pain

The Roland-Morris disability index (RMDI) for acute LBP was utilised in this study (Appendix M). It involved the participants placing a check mark next to the statement that most applied to them. The scores are calculated by adding the number of checked statements, the maximum score that can be achieved is 24 (maximum disability) and the lowest score is zero (no disability) (Roland and Fairbank, 2000).

Reliability and validity of this scale was originally determined by Roland and Morris (1983) and since then four studies (Brouwer *et al.,* 2004; Chansinirukar *et al.,* 2005; Frost *et al.,* 2008 and Schiphorst-Preuper *et al.,* 2008) have reported that the RMDI has high reliability in test-retest performance of 0.91 (same day), 0.88 (up to one week) and 0.83 (up to three weeks). A clinically significant change in the RMDI is 3.5 points, which is 14.6% when converted to a percentage (Ostelo and de Vet, 2005).

Objective and subjective measurements were taken prior to the initial treatment, on the second visit, which took place within three to four days of the initial visit and then

again at the third visit which took place within one week of the initial visit (Appendix K)

3.5 Interventions

The researcher contacted HEALTHtech Investments (Pty) Ltd/(Edms) Bpk/Co. /Mpy (Healthtech House, Cnr. Douglas and Old Pretoria Road, Midrand, South Africa; PO Box 12285, Vorna Valley, 1686) to request to conduct research on a cooling gel with herbal extracts (Reg. No. 1999/018375/07) that they manufacture. On agreeing to the research protocol (Appendix M) the company manufactured the three gels to ensure that they all looked and smelled the same. The company packaged the gels, removing all commercially identifying labels, and then labelled them with either the letter A, B or C in order for them to be administered correctly. These procedures were instituted to ensure that the researcher and the participants were un-aware of which gel they were receiving. The company only disclosed the allocation of gels once statistical analyses had been performed.

3.5.1 Gel application

All participants irrespective of group were administered an initial application of the gel performed by the researcher where a level tablespoon of the gel was applied to the area between the lower ribcage and the upper buttock bilaterally. The gel was massaged into the skin using a flat hand in circular motions for 30 seconds.

Consecutive applications of the gel were performed by the participants whereby they were to apply a level table spoon of the gel in a similar manner as performed by the researcher, at least three times a day for the duration of the study. In order to monitor the usage, a compliance diary was given to each participant, where they recorded the time that they had used the gel each day. The directions as to how the gel should be applied, as described above, were printed on the diary.

3.5.2 Treatment duration

Treatment was administered three times a day over six consecutive days. After the initial application of the gel by the researcher the participant was instructed to administer two more applications that day, thereafter the gel needed to be applied three times a day. This particular protocol was used based on a previous study by

Zhang *et al.,* (2008) which specified that participants were to apply the gel three times a day. In the present study, the treatment had to be applied over six consecutive days due to the natural history of acute low back pain which starts to improve after two weeks without any intervention being administered (Hills, 2012). Thus to ensure that the gel was applied and measurements were taken before the onset of natural history, only participants with a pain duration up to one week were included in the study. Furthermore, this study protocol is in line with the protocol laid out by Moody (2010), who suggests that a topical medication containing low concentrations of menthol should be applied three to four times a day, for no longer than seven days.

3.6. Research procedure

The Chiropractic Clinic reception staffs received the gels from the company and were responsible for allocating the participants according to the randomized allocation chart. This further ensured that the researcher remained blinded. The allocation was concealed from the participant and the researcher, thus the researcher made use of the clinic receptionist to assist in handing the correct tub of gel to the researcher and ensuring the allocation chart remained concealed from the researcher (Appendix N).

On being accepted into the study and following completion of the subjective and objective measurements, the researcher collected the gel labelled A, B or C from the clinic reception staff. The participant was positioned prone on the examination bed and the gel was administered as outlined in 3.5.1

The participant then re-dressed and, before leaving the consultation room, received a tub of gel and a plastic disposable spoon from the researcher with an explanation of how to apply the gel at home. The participant was shown how to complete a daily compliance diary, and was instructed to inform the researcher should they experience any adverse reactions to the gel.

The researcher then booked two follow up consultations within one week of the first consultation. The second consultation took place three or four days after Consultation One, where the researcher enquired about any adverse reactions or difficulties the participant experienced when using the gel at home, after which follow

up measurements were taken by the researcher and the final consultation took place one week after Consultation One where the researcher took the final measurements and collected the completed compliance diary used to note the gel applications per day.

3.7 Data analysis

On the completion of the study the data was extracted from the data collection sheet. Where necessary it was coded and then recorded in an excel spreadsheet for analysis. In order to analyse the data from the NRS and the RMDI, raw scores were converted to percentages. The pressure pain threshold measurements were recorded as raw scores in kg/cm^2.

SPSS version 21 was used to analyse the data. A p value < 0.05, confidence interval of 95%, was considered as statistically significant. Descriptive statistics were used to summarise and describe the data. Inferential statistics were used to assess for any significant differences with-in and between the groups. One way ANOVA was used for continuous data such as age, pain, pressure pain and disability measures. Chi square tests were used to compare categorical variables like gender and race between groups. Repeated measures ANOVA were used to determine the effect of the interventions for both inter- and intra-group analysis. A significant time by group interaction signified a significant treatment effect (Esterhuizen, 2014).

3.8 Ethical considerations

Permission to place advertisements at different sites was obtained prior to advertisement placement.

A Memorandum of Understanding between HEALTHTech Labs Pty (Ltd) was signed, in accordance with the relevant protocols of Durban University of Technology, Technology Innovation and Partnerships Department (Appendix O).

The research procedure was explained to the participant before they agreed to partake in the study and it was explained that the participant was able to withdraw at any point. To ensure the autonomy of the participants, written informed consent was obtained from every participant on agreeing to partake in the study.

An agreement was made with the receptionist at the Chiropractic Day Clinic (CDC) to be the research assistant (Appendix N)

In line with the ethical principle of beneficence, the study was deemed to be of benefit to manual therapists and persons self-selecting to utilize this gel, as the result would determine if there is a benefit in using the gel for acute low back pain.

In order to ensure that the placebo group received were not disadvantaged they received two free treatments, at the DUT CDC, on completing the study. The treatments were administered by a senior chiropractic student overseen by a qualified clinician.

In line with the principles of non-maleficence, the participants were correctly instructed regarding the use of the gels and were informed that they were only for external use. They were requested to stop application of the gel if they developed any adverse reactions such as itching, redness or any form of irritation on the surface of their skin. The researcher would have recorded any such adverse events. There have to date been no adverse effects reported from utilizing the gel.

CHAPTER FOUR : RESULTS

4.1 Consort diagram

The consort diagram, Figure 4.1, shows the number of respondents to the study, the number of participants allocated into the intervention groups, those who were excluded and lost due to drop outs and how many completed the study.

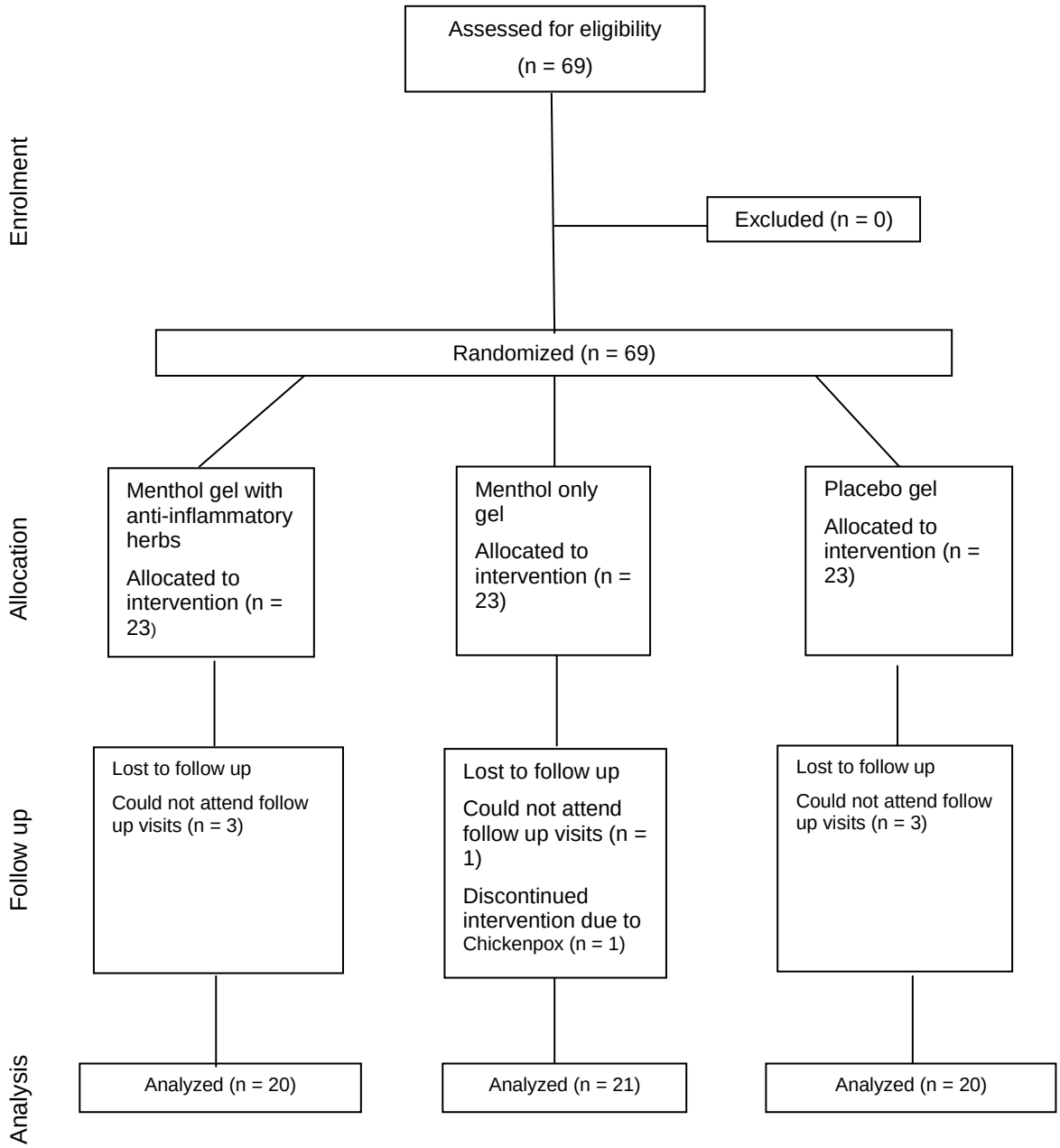


Figure 0.1: The consort diagram

4.2 Participant characteristics

4.2.1 Gender

There were more female than male participants in this study, as seen in Figure 4.2, with no significant differences (p = 0.372; Chi square test) being found at baseline between the groups in terms of gender.

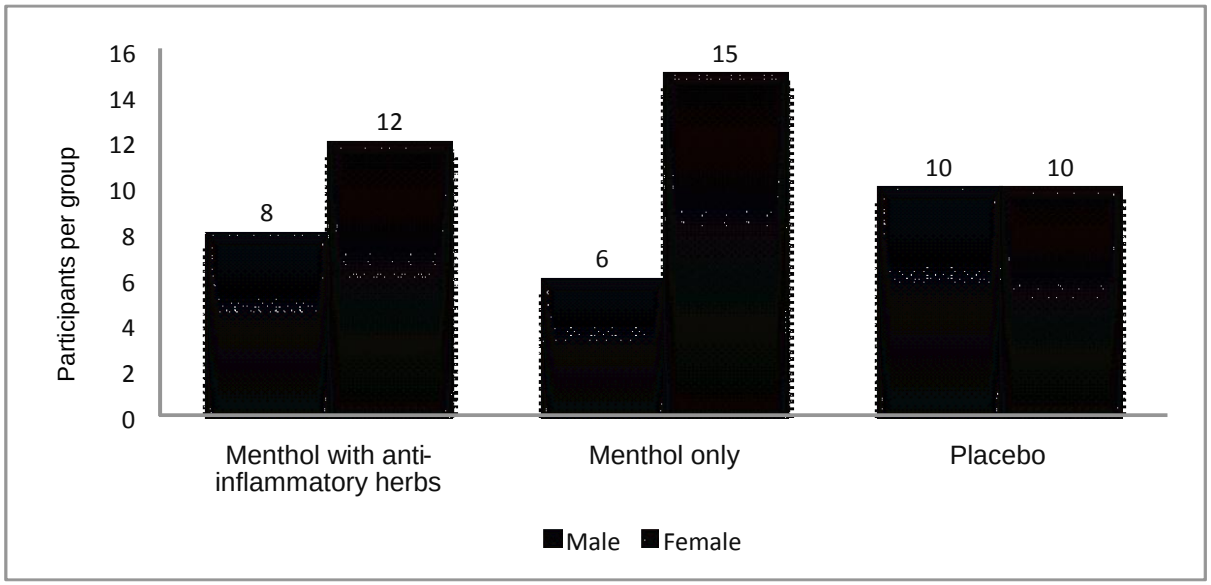


Figure 0.2: Gender distribution per group (n=61)

4.2.2 Race

The participants represented the four main race groups of the greater eThekwini Municipality as seen in Table 4.1, with no significant difference (p = 0.422; Chi squared test), being noted between the race groups at baseline.

Table 0.1: Racial distribution of participants (n=61)

Group	N	Black		Coloured		Indian		White	
		N	%	N	%	N	%	N	%
Menthol with anti-inflammatory herbs	20	6	30	3	15	4	20	7	35
Menthol	21	9	42.9	5	23.8	4	19	3	14.3
Placebo	20	12	60	3	15	2	10	3	15
Total	61	27	44.3	11	18	10	16.4	13	21.3

4.2.3 Age

The age range of the respondents was from 18 to 39 years of age. The mean age of the participants in the groups was 27 years for the menthol with anti-inflammatory herbs (SD±6), and the placebo group (SD±7), and 26 years (SD±5) for the menthol group. There were no significant difference found between the groups (p=0.963; Chi square test) in terms of age.

4.2.4 Height, weight and body mass index (BMI)

There were no significant differences between the groups in terms of height (p = 0.584; Chi squared test), weight (p = 0.730; Chi squared test) and BMI (p = 0.987; Chi squared test) as seen in Figure 4.3 at baseline measurements. The participants in all three groups were found to be overweight according to the BMI classification system.

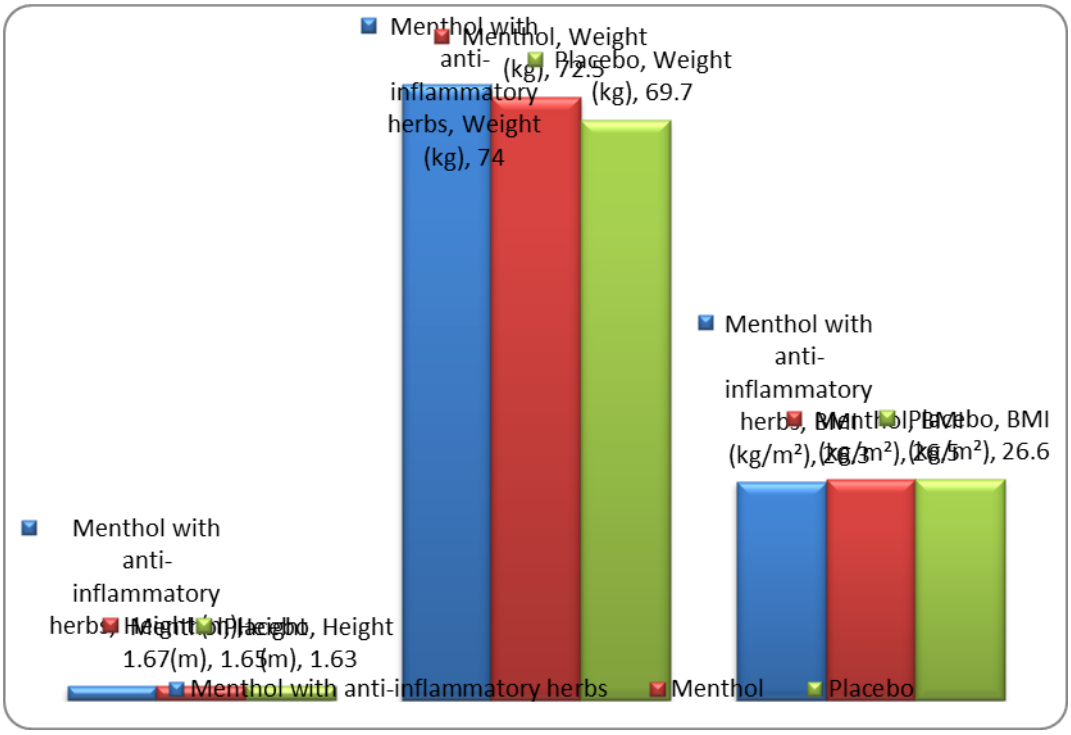


Figure 0.3: Mean height, weight and BMI per group

4.2.5 Occupation

As can be seen from Table 4.2, the participants in this study had a variety of occupations, with students being the predominant occupation.

Table 0.2: Occupations of participants by group

Occupation	Menthol with anti-inflammatory herbs	Menthol only	Placebo	Total
Students	6	9	11	26
Office Workers	3	2	1	6
Factory Workers	1	2	1	4
Health Care Workers	2	2	2	6
Retail Sector	4	0	0	4
Food Industry	1	0	3	4
Sportsman	0	0	2	2
Policing Officer	1	1	0	2
Self-employed	1	1	0	2
Navigational Officer	1	0	0	1
Croupiers	0	2	0	2
Educators	0	2	0	2
Total	20	21	20	61

4.3 Pain rating

There were no significant differences in pain rating between the groups ($p = 0.706$, one way ANOVA) at baseline, making the groups comparable. The mean pain rating for the three groups classified them as having a moderate degree of pain. Intra-group analysis, using repeated measures ANOVA, showed that each group had a statistically significant change over time, as seen in Table 4.3, with no statistically significant difference being observed between the groups over time ($p = 0.95$, repeated measures ANOVA). This shows that all three interventions resulted in an improvement of pain over the study duration with no intervention being superior to the other in decreasing pain. Similarly, all groups showed a clinically significant improvement in pain (a minimum change of 20 percent) over the duration of the study, with pain improving from moderate to mild in nature.

Table 0.3: Pain rating scores per group

Group	Pre- Intervention			Mid- Intervention				Post Intervention				p-value
	Mean	SD (±)	CI (95%)	Mean	SD (±)	CI (95%)	Clinical change	Mean	SD (±)	CI (95%)	Clinical change	
Menthol with anti-inflammatory herbs	48	2.66	42.68 - 53.32	32.5	3.57	25.3-39.64	15.5	20	3.65	12.7-27.3	28	<0.001
Menthol	47.62	2.59	42.43-52.81	35.71	3.48	28.7-42.68	11.91	21.91	3.56	14.78-29.03	25.71	<0.001
Placebo	50.5	2.66	45.18-55.82	36.5	3.56	29.3-43.64	14	22	3.65	14.70-29.30	28.5	<0.001

4.4 Disability

There were no significant differences in terms of disability (p = 0.419, one way ANOVA) at baseline, making the groups comparable. The participants were classified as having mild disability. Intra-group analysis, using repeated measures ANOVA, showed that each group had a statistically significant improvement in disability over time as seen in Table 4.4. However, there was no statistically significant change over time observed between the groups (p = 0.903 repeated measures ANOVA). This result shows that all three interventions resulted in an equal improvement in disability. No clinically significant improvement in terms of disability occurred in any of the groups.

Table 0.4: Disability per group

Group	Pre- Intervention			Mid- Intervention				Post Intervention				p-value
	Mean	SD (±)	CI (95%)	Mean	SD (±)	CI (95%)	Clinical change	Mean	SD (±)	CI (95%)	Clinical change	
Menthol with anti-inflammatory herbs	21.88	3.13	15.61-28.15	14.78	2.7	9.39-20.18	7.1	9.17	2.42	4.32-14.02	12.71	<0.001
Menthol	21.02	3.06	14.91-27.14	16.45	2.63	11.19-21.72	4.57	9.53	2.36	4.80-14.26	11.49	<0.001
Placebo	26.46	3.13	20.19-32.73	18.95	2.7	13.55-24.34	7.51	13.12	2.42	8.27-17.96	13.34	0.01

4.5 Pressure-pain threshold

There was no statistically significant differences between the groups in terms of pressure-pain threshold (p = 0.394 one way ANOVA) at baseline. Intra-group analysis, using repeated measures ANOVA, showed that the pressure-pain threshold improved significantly over the study duration in each group, as seen in Table 4.5. There were no statistical (p = 0.824 repeated measures ANOVA) or clinically significant differences observed between the groups over time. This finding indicates that all three interventions resulted in an increase in pressure pain tolerance over the duration of the study.

Table 0.5: Pressure Pain Threshold per Group

Group	Pre- Intervention			Mid- Intervention				Post Intervention				p-value
	Mean	SD (±)	CI(95 %)	Mean	SD (±)	CI (95%)	Clinical Change	Mean	SD (±)	CI(95%)	Clinical change	
Menthol with anti-inflammatory herbs	4.87	0.35	4.16-5.57	5.18	0.36	4.46-5.89	0.23	6.19	0.38	5.43-6.94	1.32	<0.001
Menthol	4.88	0.34	4.19-5.57	5.39	0.35	4.7-6.09	0.51	6.25	0.37	5.52-6.99	1.37	0.006
Placebo	5.47	0.35	4.76-6.17	5.87	0.36	5.15-6.58	0.4	6.5	0.38	5.75-7.25	1.03	0.015

4.6 Correction of BMI data to assess its effect on the outcomes

Using an ANCOVA to correct for BMI, BMI was shown to have no influence on pain rating (p = 0.896), disability (p = 0.143) and pressure-pain thresholds (p = 0.143) overtime.

CHAPTER FIVE : DISCUSSION

5.1 Participant characteristics

5.1.1 Gender, race and age

It has been documented that the female gender has a higher prevalence (Hoy *et al.,* 2010) with more frequent episodes (Woznicki, 2014) of low back pain than males. Females have also been shown to report more pain and disability from musculoskeletal disorders in comparison to males and as a result, seek healthcare more often for these conditions (Stenberg and Ahlgren, 2010). In line with this there were more females than males in this study population. However, the gender distribution between the groups was not significantly different ($p = 0.372$), indicating that gender would have had little influence on the results of the study.

South Africa has a diverse population as seen by the participants in this study. The four main race groups were represented, with a predominance of black participants. Advertisements were placed in multiracial areas such as universities, shopping malls, sports clubs and local gyms. Race has been shown to have little effect on the development of acute low back pain (De Wet, 2003; Plesh *et al.,* 2011). In this study no significant differences observed between the groups in terms of race ($p = 0.422$).

Age was a controlled variable in this study to ensure that patients were skeletally mature and to decrease the chance of patients presenting with pain due to sacroilliac or spinal degeneration. The age distribution across the three groups was similar with no significant difference ($p = 0.963$) between groups, indicating that age would not have affected the results. The mean age of the participants was relatively young (26 years of age, SD±5); this may have been due to the study location which was at the Chiropractic Day Clinic, which is located at the Durban University of Technology, making the study accessible to a student population. This may also mean that the participants were more likely to heal faster, as they would be less likely to have an acute on chronic presentation than an older population.

5.1.2 Height, weight and body mass index (BMI)

Height, weight and BMI were not controlled in this study and the evidence regarding the development of low back pain and BMI is conflicting. A meta-analysis (n = 95) of the literature regarding the association between BMI and low back pain, found that overweight and obese individuals may be at a greater risk to develop low back pain (Shiri *et al.,* 2009). Mirtz and Greene (2005) found that a BMI of less than 30kg/m² was associated with a minimal risk of low back pain and a BMI of greater than 30kg/m² was associated with a moderate risk of low back pain. In general, greater BMI measurements are correlated with greater levels of functional disability in patients (Tobin *et al.,* 2009).

In contrast, Viester *et al.* (2013) who investigated the relationship between BMI and the prevalence of musculoskeletal disorders (n = 44 793), found that neither the improvement nor the occurrence of low back pain was more prevalent in overweight and obese individuals. In a prospective cohort study by Jensen *et al.,* (2012), it was noted that there was no increased risk of low back pain in overweight or obese female health care workers (n = 2235). However, individuals with taller heights may be more prone to low back pain as taller individuals may have a potential risk for disc instability under external loading (Duthey, 2013).

No significant differences were noted between the groups in terms of height ($p = 0.584$), weight ($p = 0.730$) and BMI ($p = 0.987$). However, all the participants were classified as being overweight by the BMI (see Table 2.4). A noted limitation of the BMI measurement is that it does not distinguish whether the source of the measurement of weight is lean muscle mass or fat mass (Han *et al.,* 1997).

Overweight individuals have also been shown to have greater values in skinfold thickness and a greater amount of subcutaneous fat (Sakamaki *et al.,* 2013). The gels utilised in this study were applied topically, however, according to Kolarsick *et al.* (2011) skinfold thickness may no effect on the absorption of topically applied medication as the absorption of these medications take place in the vascularized dermis which is relatively the same thickness amongst individuals of varying BMI measurements (Laurent *et al.,* 2007). Thus, although BMI was not controlled in this study, the BMI was similar between the groups and its impact on the results would

have been negligible. It is unclear if the participants had been in a normal BMI range if the results would have been different.

5.1.3 Occupation

The participants in this study had a variety of occupations as noted in Table 4.3, with students being the predominant occupation. Student populations have been documented to experience high rates of low back pain (Moroder *et al.,* 2011), which may be due to the "prolonged sitting and looking down" posture adopted by most university students when attending lectures and studying (Nyland and Grimmer, 2003). The current study was conducted at a university and the advertisements were placed at other universities in the surrounding areas, thus the study was easily accessible to this population. This would have resulted in an increased number of students responding to the advertisements and thus participating in the study.

The participants in this study were not given time off from work or from attending lectures, therefore they still performed their normal activities; it is possible that incorrect ergonomic positioning and manual labour may have placed demands on the low back, leading to an exacerbation of their low back pain (Morris, 2006). Although "active rest" is recommended for acute low back pain patients (Liebenson, 2006), it may have affected their response to the administration of the cooling gels.

5.2 Discussion of the results

5.2.1 Pain rating

Acute low back pain can be rated as severe, moderate or mild (Hanley *et al.,* 2006), depending on the mechanism of injury, the pain intensity and the patient's pain tolerance (Mannion *et al.,* 2007). In order to participate in this study the participants had to rate their pain between three and six on a pain rating scale, indicating moderate pain (Hanley *et al.,* 2006). This was implemented to ensure homogeneity amongst the participants, and resulted in the groups being comparable at baseline assessment. Following the interventions all groups showed statistical and clinically significant improvements in pain ($p < 0.001$), thus neither the cooling gel with anti-inflammatory herbs nor the menthol only gel was superior to placebo.

These results were in contradiction to Harper (2010) who found that the same menthol and anti-inflammatory herb gel used in this study, a menthol only gel and an ice pack had a similar rate of pain improvement which was superior to placebo in the treatment of grade one and two acute ankle sprains. This raises a question as to whether the depth of the site of injury is a factor when applying cooling gels.

Airaksinen *et al.* (2003) found that a cooling gel containing 3.5 percent menthol and 8 percent ethanol was superior to a placebo gel when treating soft tissue injuries of the hand, knee, leg, foot and ankle with measurements being recorded at days seven, 14 and 28. Pain rating scores at seven days in the trial by Airaksinen *et al.* (2003) showed a significant difference ($p < 0.001$) between the groups, whereas in the current study, the pain rating scores within the same time frame showed no difference ($p = 0.95$) between the intervention groups.

Both Airaksinen *et al.* (2003) and Harper (2010) made use of extremity sites in their studies, which have generally less tissue depth in comparison to the low back. It has been noted that the depth of tissues causing pain at different sites around the body (Hendriks, 2005) can affect the efficacy of cryotherapy applied as cooling of the tissues becomes more difficult at greater tissue depths (Heinrichs, 2004; Klein, 2013). It is uncertain whether cooling gels containing menthol are able to bring about therapeutic effects at varying tissue depths and further investigation into this is required.

In addition, the mechanism of injury of mechanical low back pain and soft tissue injuries such as sprains of the foot and ankle are different. When the ankle joint is placed in a loose packed position, such as plantarflexion or inversion (Wolfe *et al.,* 2001; Lynch*,* 2002), there is dissociation from the bony structures such as the talus (Anderson, 2002). Thus the ligaments are now required to play a greater role in the stability of the joint, and are more susceptible to injury (Wolfe *et al.,* 2001). The injury that results in an ankle sprain can be described as “rolling over” the lateral aspect of the ankle, when the joint is placed in this vulnerable position and is regarded as a major traumatic singular event with marked signs of inflammation such as oedema, pain and redness (Lynch, 2002).

Mechanical low back pain may be attributed to a number of minor traumatic events such as repeated small loads (bending) or sustained loading (prolonged sitting). The

motor control system functions well under a load because the muscles are able to stabilize the joints by becoming taut. However, under prolonged strain, ligaments, joint capsules and intervertebral discs may undergo creep. The structures of the low back become vulnerable as they no longer offer stability effectively, and are liable to injury if an unexpected minimal load is applied (Liebenson, 2000). The contrast to Harper's (2010) findings may be due to the gels diminishing the oedema and pain immediately produced by the major tissue failure whereas it may be less effective in the healing of prolonged minor trivial trauma occurring at a deeper level.

Another consideration is that of the quantity of menthol utilized in the cooling gels. The menthol and anti-inflammatory herbs and the menthol gels utilized in this study contained 0.76 percent m/v of menthol in a 500g tub of gel (Gerber, 2014) compared to the a topical gel investigated by Airaksinen *et al.,* (2003) which contained 3.5 percent menthol. The manufacturers of the gel stated that the rationale for using a menthol concentration of 0.76 percent is that this concentration was perceived to produce the greatest amount of cooling at the lowest level of discomfort (Gerber 2014). Perhaps greater concentrations of menthol are required to elicit similar therapeutic effects in tissues with a greater subcutaneous tissue depth.

It has been noted that concentrations of one percent or less may suppress cutaneous sensory receptors whereas concentrations of 1.26 to 16 percent would stimulate sensory receptors and act as a counter-irritant (Patel *et al.,* 2007). Stimulating sensory receptors and acting as a counter-irritant may activate the large-diameter nerve fibres to override the smaller nociceptive nerve fibres and essentially block nociceptive information from reaching the central nervous system (Page and Mackison, 2007). This is known as the gate control theory which was first proposed by Melzack and Wall in 1965. This may explain the mechanism by which menthol of higher concentrations may be able to bring about systemic pain reduction.

Biofreeze® (a herbal gel containing 3.5 percent menthol) was compared to ice to determine its effect on radial artery blood flow. After five minutes, Biofreeze® resulted in a significant ($p = < 0.05$) decrease in blood volume whereas this same effect only occurred after 20 minutes of ice application. However the reduction of blood flow was not sustained at 10, 15 or 20 minutes after the application of menthol, making it a fast acting but short lived effect. This effect is most likely due to menthol

acting through neuronal mechanisms by stimulating transient receptor potential M8 which belongs to a group of excitory ion channels (Patel *et al.,* 2007). Thus the concentration of the menthol used in this study may have been too small to bring about the beneficial effects noted when using larger concentrations. A follow up study should investigate the effect of the gels used in this study to determine their effect, if any, on radial artery blood flow.

Menthol has also shown to enhance the penetration of added ingredients such as topical anaesthetics (Liu *et al.,* 2005). Anti-inflammatory herbs have also been added to these gels. The cooling gel used in this study contained less than 0.5 percent anti-inflammatory herbal extracts, which may have been a sufficient quantity to bring about an effect on superficial areas of the body (Harper, 2010). However, this concentration may not be enough to bring about anti-inflammatory effects in areas of deeper tissue depth. Further investigation into the concentration of anti-inflammatory herbs necessary to elicit a therapeutic effect at varying tissue depth is required.

The mechanism of placebo must also be considered as it has an important influence on therapeutic outcomes such as pain reduction (Benedetti *et al.,* 2005). A reduction in pain following the use of a placebo is possibly due to the involvement of the endogenous opioid system in the brain; therefore the same pathways that are involved in placebo are also involved in pain reducing mechanisms (Meissner *et al.,* 2010). The placebo gel in this study did not contain any active ingredients nor was it cold thus it did not act in the same mechanism pathway as the other two groups but rather through subjective psychological mechanisms. Participants were unaware of allocation group, and the gels were manufactured to be identical in smell and appearance making it difficult to distinguish between them. The act of having to rub a gel onto the skin daily in itself was a treatment. A five minute massage is considered to be the minimum time required to bring about a physiological response due to the massage (Tanaka *et al.,* 2002); thus, a 30 second massage, which was the duration of the massage of the participants in this study, would not have produced a physiological reaction due to the massage alone. Nevertheless, as seen in these results, the placebo effect was powerful.

5.2.2 Disability

Acute low back pain sufferers have reported difficulty in performing activities of daily living (Leveille *et al.,* 1999). Difficulty in performing these activities is known as disability (Deeg, 2013). It is a common outcome measure in low back pain and is measured by self-reported questionnaires (Lin *et al.,* 2011). The participants in this study reported mild disability, indicating that their activities of daily living were not severely hampered by their pain, and over the duration of the study the reported disability decreased to almost negligible. All the groups were comparable at baseline ($p = 0.419$) and they improved at the same rate over time with no group being superior.

Similar results were noted by Zhang *et al.* (2008) where a cooling gel, Biofreeze®, was used in combination with chiropractic manipulation (CM) and compared to CM alone in acute low back pain participants. They found no significant difference in disability changes between the groups.

Disability measures such as the Roland Morris Disability Index (RMDI) are subjective measurement tools and rely on a patient's self-reporting to assess the impact of low back pain on daily activities (Davidson and Keating, 2002) which may not always be reliable because non-applicable responses, which are not listed in the index, may not be reported and thus the resulting measurement may not be a true reflection of the patient's disability (Roland and Fairbank, 2000). However disability is an important aspect of low back pain and can influence whether it becomes chronic or not (Liebenson, 2006).

The natural history of low back pain needs to be considered, as it has been documented that it will naturally improve in two weeks (Hills, 2012). This study was designed to complete the treatment of acute low back pain before the passing of the two week natural history period. However it is possible that the improvements in disability may have occurred due to the passing of time or the effect of seeking treatment for acute low back pain.

5.2.3 Pressure-pain threshold (PPT)

All the groups had significant improvements ($p < 0.05$) in pressure-pain thresholds but none were clinically significant (an increase in PPT of 1.5 kg/cm^2) as noted in

Table 4.6. These results are contradictory to Avrahami *et al.* (2012) who found that three different creams and two roll-on gels containing menthol were superior to the placebo gel in terms of improving PPTs in neck pain participants. Harper (2010) also found that a menthol gel and a menthol gel with anti-inflammatory herbs were more effective than placebo in increasing the PPT in grade one and two ankle sprains. Discrepancies in these findings, as previously discussed, may be attributed to tissue depth; both the neck and ankle are relatively superficial when compared to the low back region.

CHAPTER SIX : CONCLUSION AND RECOMMENDATIONS

6.1 Conclusions

Cooling gels are often used in an athletic and clinical setting as they provide a convenient and safe method of application and reportedly decrease the inflammation and pain associated with acute soft tissue injuries. Several studies have investigated the effect of cooling gels with contradictory results. The menthol cooling gel with anti-inflammatory herbs utilised in this study is widely available in South Africa, and is utilised frequently for musculoskeletal conditions such as low back pain.

The results of this study found that there were no significant differences between the groups, indicating that the menthol cooling gel with anti-inflammatory herbs was no more effective than menthol or a placebo gel in reducing pain, disability and increasing pressure-pain threshold levels. This is in contrast to a previous study investigating the same gel in a different musculoskeletal condition. The study highlighted the possibility that different areas of the body, depending on tissue depth, may require different concentrations of menthol in order to elicit an effect.

From the results of this study the null hypothesis was un-able to be rejected as there was no statistically significant difference between the three groups in terms of pain, disability and pain tolerance. The alternate hypothesis was rejected as the menthol combined with anti-inflammatory herbs gel did not show a greater improvement in terms of pain, disability and pain tolerance when compared to the menthol and placebo gel.

6.2 Recommendations

The recommendations arising from the study are listed below.

6.2.1 Recommendations for future research

A similar study should be conducted investigating the effect of cooling gels containing varying quantities of menthol and their effect on radial artery blood flow in

order to establish the appropriate concentration of menthol which causes a therapeutic effect.

Following the above the cooling gel should then be tested in various musculoskeletal conditions and locations, with varying tissue depths, to establish its effectiveness.

Further investigation into the anti-inflammatory herbs used in this gel needs to be conducted to determine if the quantity is sufficient to elicit the desired effect.

Activities of daily living (ADL) were not controlled in this study. It is unknown if these confounding variables may have had an effect on the outcome of the results. It is recommended that future research should control for these variables. This may be possible by utilising a defined study population e.g. students or athletes.

The Roland-Morris Disability Questionnaire has limitations in its design, as difficulty with activities which are not listed in the index, may not be reported and thus the resulting measurement may not be a true reflection of the patient's disability. The patient-specific functional scale has been identified as being more responsive in patients with mild to moderate levels of disability (Hall *et al.,* 2011). Future studies including participants with lower levels of disability should consider utilising this scale.

For propriety reasons, the exact concentration of the known ingredients could not be listed and there were unknown herbal ingredients also added to the gel. Therefore, the half-life of these ingredients could not be identified. It is recommended that future research take the half-life of known ingredients into consideration when designing the study protocol as the amount of time that substances remain active in the systemic circulation may have an effect on the results.

6.2.2 Recommendations for clinical practice

Clinicians should be cautious when recommending the use of the menthol containing cooling gels in patients with acute mechanical low back pain, pending further research, as the results of this study do not substantiate their use, other than for placebo, in this condition.

6.3 Study limitations

Patient compliance in utilizing and applying the gel may have been a limitation of the study. To circumvent this, the participants were required to complete a diary. The diary was used to record the gel application between follow up consultations in an attempt to ensure that the procedure was performed however it is possible that the participants either under or over utilised the gel which may have affected the results.

REFERENCE LIST

Airaksinen, O.V., Kyrklund, N., Latvala, K., Kouri, J.P., Grönblad, M. and Kolari, P. 2003. Efficacy of cold gel for soft tissue Injuries: a prospective randomized double-blinded trial. *American journal of sports medicine*, 31(5):680-64.

Allen, R. 2006. Physical agents used in the management of chronic pain by physical therapists. *Physical medicine and rehabilitation clinics of North America*,17:315-345.

Algarfly, A.A. and George, K.P. 2007. The effect of cryotherapy on nerve cell velocity, pain threshold and pain tolerance. *British journal of sports medicine*, 41:365-369.

Amirlak, B. 2013. *Skin anatomy* (online). Available at: http://emedicine.medscape.com/article/1294744-overview. [Accessed on 15 May 2014.]

Andersen, H.H., Olsen, R.V., Moller, H.G., Eskelund, P., Gazerami, P and Arendt-Nielsen, L.2013. A review of topical high concentration L-mentholas a transitional model of cold allodynia and hyperalgesia *European journal of pain*.p1-11.

Anderson, S.J. 2002. Acute ankle sprain: key to diagnosis and return to play. *The physician and sports medicine*, 30(12):29-35.

Andrews, J.R., Harrelson, G.L and Wilk, K.E. 2014. *Physical rehabilitation of the injured athlete*. 4th ed. Philadelphia, PA: Elsevier Saunders.

Anselmo, P. 2003. Arnica (online). Available at: http://www.ucdenver.edu?academics/colleges/pharmacy/current/students/OnCampusPharmDStudents/ExperimentalProgram/Documents/nutr-monographs/Monographs-arnica.pdf [Accessed date 25 June 2014.]

Antonaci, F., Sand, T. and Lucas, G. 1998. Pressure algometry in healthy subjects: inter-examiner reliability. *Scandanavian journal of rehabilitative medicine*, 30:3-8.

Assendelft, W., Morton, S., Yu, E., Suttorp, M. and Shekelle, P. 2004. Spinal manipulative therapy for low back pain. *American college of physicians,* 138(1):873-879.

Atlas, S.J. and Deyo, R.A. 2001. Evaluating and managing acute low back pain in the primary care setting. *Journal of general internal medicine*, 16(2):120-131.

Avrahami, D., Hammond, A., Higgins, C. and Vernon, H. 2012. A randomized double-blinded placebo-controlled comparative clinical study of five over-the-counter non-pharmacological topical analgesics for myofascial pain: single session findings. *Chiropractic and manual therapies,* 20(7):1-6.

Balagué, F., Mannion, A.F., Pellisé,F. and Cedraschi, C. 2012. Non-specific low back pain. *Lancet*, 379:482-491.

Baldwin, J.F. 2014. Lumbar (intervertebral) disk disorders. Available at: http://emedicine.medscape.com/article/827016-overview#aw2aab6b2b5. [Accessed on 18 November 2014.]

Beck, M. 2010. *Theory and practice of therapeutic massage.* 5th ed. Clifton Park, N.Y.: Cengage Learning. p463.

Benedetti, F., Mayberg, H.S., Wagner, T.D., Stohler, C.S and Zubieta, J. 2005. Neurobiological mechanism of the placebo effect. *The journal of neuroscience,* 25(45):10390-10402.

Bernard, T.N. and Cassidy, J.D. 1992. Sacroilliac syndrome: pathophysiology, diagnosis and management. In: Frymoyer, J.D. The adult spine: principles and practice. New York: Raven. p2107.

Bertalanffy, A., Kober, A, Bertalanffy, P., Gustorff, B., Gore, O., Adel, S. and

Hoerauf, K. 2005. Transcutaneous electrical nerve stimulation reduces acute low back pain during emergency transport. *Academic emergency medicine,* 12(7):607-11.

Best, T. 1997. Soft issue injuries and muscle tears. *Clinical sports medicine,* 16:419-434.

Bharate, S.S. and Bharate, S.B. 2012. Modulation of thermoreceptors TRPM8 by cooling compounds*. ACS chemical neuroscience,* 3(4):248-267.

Bhattacharya, D. 2006. *Research methodology*. 2nd ed. New Delhi: Excel Books. p41.

Bijur, P., Silver, W., Gallagher, J. 2001. Reliability of the visual analog scale for the measurement of acute pain. *Academy of emergency medicine,* 8(12):1153-1156.

Bishop, B., Greenstein, J. and Topp, B. 2009. Effects of Biofreeze versus ice on acute non-complicated neck pain. *Clinical chiropractic*, 14(4):153-154.

Bissolotti, L., Gaffurini, P and Meier, R.2013. BTS – walk:clinical notebook.2nd edition.Italy: BTS Bioengineering

Bleakley, C., McDonough, S. and MacAuley, D. 2004. The use of ice in the treatment of acute soft tissue injury. *American journal of sports medicine,* 32(1):251-261.

Bleakley, C., McDonough, S. and MacAuley. 2006. Cryotherapy for acute ankle sprains: a randomised controlled study of two different icing protocols. *British journal of sports medicine*, 40:700-705.

Bleakley, C.M. and Davison, G.W. 2010. Cryotherapy and inflammation: evidence beyond the cardinal signs. *Physical therapy reviews,* 15(6):430-434.

Bogduk, N. 2005. *Clinical anatomy of the lumbar spine and sacrum*. 4th ed. Edinburgh: Elsevier Churchill Livingstone. p 39-48, 126 and 143.

Bootman, M., Lipp, P. and Berridge, M.J. 2001. The organisation and function of local calicium ion channels. *Journal of cellular science,* 114:2213-2222.

Brennan, G., Shafat, A., Donncha, C. and Vekins, C. 2007. Low Back Pain in Physically Demanding College Academic Programs: A Questionnaire Based Study. *BioMedical Central Musculoskeletal Disorders*, 8(67):1-8.

Bronfort, G., Haas, M., Evans, R., Leininger, B. and Triano, J. 2010. The effectiveness of manual therapies: The UK report. *Chiropractic and osteopathy,* 18(3).

Brouwer, S., Kuijer, W., Dijkstra, P.U., Goeken, L.N., Groothoff, J.W. and Geertzen, J.H. 2004. Reliability and stability of the Roland Morris Disability Questionnaire: intra class correlation and limits of agreement*. Disability rehabilitation,* 26(3):162-5.

Cameron, M. 2012. *Physical agents in rehabilitation: from research to practice*. 4th ed. St Louis: Elsevier Saunders. p129-168.

Casazza, B.A. 2012. Acute non-specific low back pain. *American family physician,* 4(85):343.

Celan, D and Turk, Z.2005.The impact of anthropometric parameters on the incidence of low back pain.*College of anthropology.*29(1):101-105

Chansirinukor, W., Maher, C., Latimer, J. and Hush, J. 2005. Comparison of the functional rating index and the 18-item Roland-Morris Disability Questionnaire: responsiveness and reliability. *Spine,* 30(1):141-5.

Chesterton, L.S., Foster, N.E. and Ross, L. 2002. Skin temperature in response to cryotherapy. *Archives physical medicine and rehabilitation*, 83:543-549.

Chesterton, L.S., Sim, J., Wright., C.C and Foster, N.E. 2007. Interater reliability of algometry in measuring pressure-pain thresholds in healthy humans, using multiple raters. *Clinical journal of pain,* 23(9):760-766.

Chien, J.J. and Bajwa, Z.H. 2008. What is mechanical back pain? *Current pain and headaches report*, 12:406-411.

Childs, J., Piva, S.R. and Fritz, J.M. 2005. Responsiveness of the numerical pain rating scale in patients with low back pain. *Spine*, (11):1331-1334.

Chiodo, A., Alvarez, D. Gregory, G., Haig, A., McGillicuddy, J., Standiford, C. and Tremper, A. 2005. Acute low back pain. Guidelines for clinical care, ambulatory. Regents of the university of Michigan.

Christensen, M. and Kollasch, M. 2005. Job analysis of chiropractic: a project report, survey analysis and summary of the practice of chiropractic within the United States. National Board of Chiropractic Examiners. University of Michigan.

Chou, R., Qaseem, A., Snow, V., Casey, D., Cross, J., Shekelle, P and Owens, D.2007. The diagnosis and treatment of low back pain: a joint clinical practice guideline from the American college of physicians and the American pain society.*Annals of Internal Medicine* 147(7):484-486

Cluett, J. 2014. Low back strain: best treatments available for low back muscle strain (online). Available at: http://orthopaedics.about.com/cs/sprainsstrains/a/lowback_2.htm. [Accessed 19 November 2014.]

Cohen, S., Argoff, C., Carragee, E. 2009. Management of low back pain. *British medical journal,* 338:100.

Cole, B. 2002. Pain management: classifying, understanding and treating pain. *Hospital physician,* p22-30.

Comerford, M.J. and Mottram, S.L. 2001. Movement and stability dysfunction: contemporary developments. *Manual therapy,* 6(1):15-26.

Coste, J., Delecoeuillerie, G., Cohen de Lara, A., Le Parc, J. and Paolaggi, J. 1994. Clinical course and prognostic factors in acute low back pain: an inception cohort study in the primary care setting. *British medical journal,* 308:577-580.

Cramer, G. and Darby, S. 2014. *Clinical anatomy of the spine, spinal cord and ANS*. 3rd ed. St Louis: Elsevier Mosby.

Dagenais, S. and Haldeman, S. 2012*. Evidence-based management of low back pain*. St Louis: Elsevier Mosby.

Dalton, M., Cameron, A.J., Zimmet, P.Z., Shaw, J.E, Jolley, D., Dunston, D.W. and Welborn, T.A. 2003. Waist circumference, waist hip ratio and BMI and their correlation with heart disease risk factors in Australian adults. *Journal of internal medicine,* 254(6):555-563.

Dasgupta, B. and Patil, P. 2012. The role of diagnostic ultrasound in the assesment of musculoskeletal disorders. *Therapeutic advances in musculoskeletal disease*, 4(5):341-355.

Davidson, M. and Keating, J. 2002. A comparison of five low back disability questionnaires: reliability and responsiveness. *Physical therapy,* 82:8-24.

Davies, C.C. and Nitz, A.J. 2009. Psychometric properties of the Roland Morris Disability Qustionnaire compared to the Oswestry Disability Index: a systematic review. *Physical therapy reviews,* 14(6):399-407.

Davy, G. 2012. How Does Cryotherapy (Ice) Help with the management of pain? (online). Available at: http://www.archealth.com.au/post/892160-how-does-cryotherapy-ice-help-with. [Accessed date 15 July 2014.]

Deeg, D.2013. Functional Limitations and Activities of daily living (online). Availiablie at http://www.lasa-vu.nl/themes/physical/functionele_beperkingen.html [Accessed on 12 March 2015]

Démarchez, M. 2010. Cutaneous vasculature (online). Available at: http://biologiedelapeau.fr/spip.php?rubrique16&lang=fr. [Accessed date 2 August 2014.]

Denegar, C., Saliba, E. and Saliba, S. 2010. Therapeutic modalities for musculoskeletal injuries. 3rd ed. Champaign, Illinois: Human Kinetics. “Cold and superficial heat.” p122-123.

Derman, E.W. and Schwellnus, M.P. 2010. Pain management in sports medicine: use and abuse of anti-Inflammatory and other agents. *South African family practitioner,* 52 (1):27-32.

De Wet, M. 2003. Low back pain in the corporate workplace. M Tech: Chiropractic dissertation. University of Johannesburg (unpublished).

Diamond, S and Borenstein, D. 2006. Chronic low back pain in a working-age adult. *Best practice and research clinical rheumatology*, 20(4):707-720.

Drugs.com. 2014. Biofreeze®. Available at: www.drugs.com/drp/biofreeze-pain-relieving-gel.html. [Accessed date 2 August 2014.]

Duthey, B. 2013. Priority medicines for Europe and the world – a public health approach to innovation (unpublished).

Eccles, R. 1994. Menthol and related cooling compounds. *Journal of pharmacology*, 46:618-630.

Ehrlich, G.E. 2003. Low back pain. *Bulletin of World Health Organization*, 81(9):671-676.

Engers, A., Jellema, P., Wensing, M., van der Windt, D.A., Grol, R. and van Tulder, M.W. 2008. Individuation patient education for low back pain. *Cochrane database systematic review,* 3(1).

Enwemeka, C., Allen, C., Avila, P., Bina, J., Konrade, J and Munns, S. 2002. Soft tissue thermodynamics before, during and after cold pack therapy. *Journal of American college of sports medcine,* 34(1):45-50.

Ernst, E. 2002. The risk-benefit profile of commonly used herbal therapies: Gingko, St John's Wort, Ginseng, Echinacea, Saw Palmetto and Kava. *Annals of internal medicine*.136(1):42-53.Esmat, T.2012.Measuring and evaluating body composition (online), Availiable at http://www.acsm.org/access-public-information/articles/2012/01/12/measuring-and-evaluating-body-composition [Accessed date 12 March 2015]

Esterhuizen, T. (tonya.esterhuizen7@gmail.com). 9 May 2013. Statistical analysis. Email to Prince, CK (prince.cleo.k@gmail.com) [Accessed date: 9 May 2013].

Esterhuizen, T. (tonya.esterhuizen7@gmail.com). 14 August 2014. Statistics. Email to Prince, CK (prince.cleo.k@gmail.com) [Accessed date : 14 August 2014].

Ferreira-Valente, M., Pais-Ribeiro, J. and Densen, M. 2011. Validity of four pain intensity scales. *Pain*, 152:2399-2404.

Finch, E., Brooks, D., Stratford, P. and Mayo, N. 2002. Physical rehabilitation outcome measures: a guide to enhanced clinical decision making. 2nd ed. Baltimore: Lippincott, Williams and Wilkins.

Fiscus, K., Kaminiski, T. and Powers, M. 2005. The change in lower limb blood flow during warm-, cold- and contrast-water therapy. *Archive of physical medicine and rehabilitation,* 86:1404-1410.

Frank, C.B. 2004. Ligament structure, physiology and function. *Journal of musculoskeletal neuronal interaction*, 4(2):199-201.

Friedman, J.H. and Dubinsky, R. 2008. The placebo effect. *Neurology,* 71:25-26.

Friedman, H., Lamb, S. and Stewart-Brown, S. 2008. Responsiveness of a Patient Specific Outcome Measure Compared With the Oswestry Disability Index Volume 2.1 and Roland and Morris Disability Questionnaire for Patients with Subacute and Chronic Low Back Pain. *Spine,* 33 (22):2450-2457.

Fundytus, M.E. 2001. Glutamate receptors and nociception: implications for the drug treatment of pain. *Central nervous system drugs*.15(1):29-58.

Furlan, A.D., Yazdi, F., Tsertsvadze, A., Gross, A., van Tulder, M., Santaguida, L., Gagnier, J., Ammendolia, C., Dryden, T., Doucette, S., Skidmore, B., Daniel, R., Ostermann, T. and Tsouros, S. 2011. A systematic review of meta-analysis of efficacy, cost effectiveness and safety of selected complementary and alternative medicine for neck and low back pain. *Evidence based complementary and alternative medicine*. p1-61.

Galeotti, N., Di Cesare Mannelli, L., Mazzanti, G., Bartolini, A and Ghelordini, C. 2002. Menthol: a natural analgesic compound. *Neuroscience letters*, 322:145-148.

Garra, G., Singer, A., Leno., R., Taira, B.R., Gupta, N., Mathaikutty, B and Thode, H.J.2010. Heat or cold packs for neck and back strain: a randomized controlled trial efficacy. *Academic emergency medicine*.17:484-489

Gawkrodger, D.J. 2002. *Dermatology: An illustrated colour text*. 3rd ed. Edinburgh: Churchill Livingstone.

Gerber, D. (david@v-tech.ac.za). 29 August 2013. Information concerning the gel. Email to Prince, CK (prince.cleo.k@gmail.com) [Accessed date : 29 August 2013].

Gerber, D (david@v-tech.ac.za). 26 November 2014. Menthol concentration of the gel. Email to Prince, CK (prince.cleo.k@gmail.com) [Accessed date 26 November 2014].

Gilchrist, R.V., Slipman, C.W., Isaac, Z., Lenron, D.A., Chou, L.H. 2002. The vascular supply of the lumbar spine: an intimate look at the lumbosacral nerve roots.

Pain physician, 5(3):288-293.

Hall, A., Maher, G., Latimer, J., Ferreira, M and Costa, L.2011.The patient specific functional scale is more responsive than the Roland Morris Disability Questionnaire when activity limitation is low. *European spine journal*.20(1):79-86

Han, T., Shouten, J., Lean, M., Seidell, J. 1997. The prevalence of low back pain and associations with body fatness, fat distribution and height. *The international journal of obesity*, 21:600-607.

Hanney, W.J., Kolber, M.J. and Beekhuizen, K.S.2009.Implications for physical activity in a population with low back pain. *American journal of lifestyle medicine.*3(1)63-70

Hanley, M., Masedi, A., Jensen, M., Cardenas, D. and Turner, J. 2006. Pain interference in people with spinal cord injury: classification of mild, moderate and severe. *The journal of pain,* 7(2):129-133.

Hayden, J., van Tulder, M., Malmivaara, A. and Koes, B. 2005. Exercise therapy for the treatment of non-specific low back pain. *Cochrane database of systematic reviews.*

Harper, S. 2010. The effectiveness of an ice pack, menthol based cooling gel, menthol based cooling gel with extracts and a placebo gel in the treatment of acute ankle sprain. M Tech: Chiropractic dissertation. Durban University of Technology (unpublished).

Heinrichs, K. 2003. Chapter 16: Superficial thermal modalities. In: Mills, D.L., Levine, D and Taylor, R. 2003. *Canine rehabilitation and physical therapy*. St Louis: Saunders Elsevier. p282-285.

Hendriks, F.M. 2005. Mechanical behaviour of human epidermal and dermal layers in vivo. Eindhoven: Technische Universiteit Eindhoven. p3-5.

Herrera, E., Sandoval, M., Camargo, D. and Salvini, T. 2011. Effect of walking and resting after three cryotherapy modalities on the recovery of sensory and motor nerve conduction velocity in healthy subjects. *The Brazilian journal of physical therapy,* 15:233-240.

Higuchi, K and Sato, T. 2002. Anatomical study of the lumbar spine innervation. *Folia morphology*, 6(2):71-79.

Hills, E.C. 2012. Mechanical lower back pain. Available at: http://www.emedicine.medscape.com. [Accessed date 20 February 2014.]

Holwerda, S.W., Trowbridge, C.A., Womochel, K.S and Keller, D.M.2013.Effects of cold modality application with static and intermittent pneumatic compression of tissue temperature and systemic cardiovascular responses. *Sports Health*.5(1)27-33

Hoy, D., Brooks,P., Blyth, F. and Ruchbinder, R. 2010. The epidemiology of low back pain. *Best practice and research of clinical rhematology*, 24:769-781.

Imanishi, N., Kishi, K., Chang, H., Nakajima, H. and Sadakazu, A. 2008. Three dimensional venous anatomy of the dermis observed using stereography. *Journal of anatomy,* 212(5):669-673.

Jayanthy, A., Sujatha, N. and Reddy, M. 2011. Measuring blood flow-techniques and applications – a review. *International journal of research and reviews in applied sciences,* 6(2):203-216.

Jellin, J., Gregory, P., Bates, F. and Hitchens, K. 2002. *Pharmacist's letter or prescriber's letter nature medicine comprehensive database*. 4th ed. Stockton: Therapeutic Research Faculty. 89-90

Jensen, J., Holtermann, A., Clausen, T., Mortensen, O., Carneiro, I. and Andersen, L. 2012. The greatest risk for low back pain among newly educated female health care workers: body weight and physical load. *BMC musculoskeletal disorders,* 13(87).

Johnson, C. 2005. Measuring pain. Visual analogue scale versus the numerical pain scale. What is the difference? (online) Available at www.ncbi.nlm.nih.gov/pmc/articles/PMC2647033. [Accessed date 10 July 2014.]

Johnston, L. 2012. Muscle and joint pain: topical anti-inflammatories and analgesics. *Professional nurse today*, 17(1):4-5.

Jones, K.R., Vojir, C.P., Hutt, E and Fink, R.2007. Determining the mild, moderate and severe equivalency across pain intensity tools in nursing home residents. *Journal of Rehabilitation and Development*.44:305-314

Jutte, L.S., Merrick, M.A., Ingersoll, C.D. and Edwards, J.E. 2001. The relationship between intramuscular temperature, skin temperature and adipose thickness during cryotherapy and rewarming. *Archive of physical medicine and rehabilitation*, 82:845 and 848.

Kahl, C. and Cleland, J. 2005. Visual analogue scale, numerical pain rating scale and the McGill pain questionnaire: An overview of psychometric properties. *Physical therapy reviews,* 10(2):123-128.

Karande, P. and Mitragatri, S. 2009. Enhancement of transdermal drug delivery via synergistic action of chemicals. *Biochimica et biophysica acta,* 1788:2362-2373.

Karnath, B. 2003. Clinical signs of low back pain. *Hospital physician,* 39(5):45-55.

Kaur, L.P. and Guleri, T.K. 2013. Topical gel: a recent approach for novel drug delivery. *Asian journal of biomedical and pharmaceutical sciences*, 3(17):1-5.

Kelley, L. and Petersen, C. 2007. *Sectional anatomy for imaging professionals*. St Louis: Elsevier.

Kinkade, S. 2007. Evaluation and treatment of acute low back pain. *American academy family physician*, 75:1181.

Kinser, A., Sands, W. and Stone, M. 2009. Reliability and validity of pressure algometer. *Journal of strength and conditioning research*, 1:312-314.

Kirkaldy-Willis, W.H. and Burton, C. 1992. *Managing low back pain*. 4th ed. New York: Churchill Livingstone.

Kirkaldy-Willis, W.H. and Bernard, T. 1999. *Managing low back pain*. 4th ed. Philadelphia: Churchill Livingstone

Kishner, S. 2014. Lumbar spine anatomy (online) Available at: http://emedicine.medscape.com/article/1899031-overview. [Accessed on 30 June 2014.]

Klein, M. 2013. Superficial heat and cold (online). Available at: www.medscape.com. [Accessed on 26 August 2014.]

Kliger, B. 2003. Echinacea. *American family physician,* 267:77-80.

Knight, K. 1985. *Cryotherapy theory: technique and physiology*. Chattanooga: Chattanooga Corporation.

Krebs, E. Carey, T.S. and Weinberger, M. 2007. Accuracy of the pain numerical rating scale as a screening test in primary care. *Journal of general internal medicine*, 10:1453-1458.

Kolarsick, P., Kolarsick, M. and Goodwin, C. 2011. Anatomy and physiology of the skin. *Journal of the dermatology nurses' association*, 3(4):203-213.

Kumar, K.M. and Ramaiah, S. 2011. Pharmacological importance of *Echinacea Purpura*. *International journal of pharmacological and biological studies,* 2(4):304.

Lanzer, P. and Topol, E.J. 2002. *Pan vascular medicine: integrated clinical management*. Springer science and business media. Berlin: Springer. p400.

Lau, J.T.F., Mao, J. and Woo, J. 2003. Ethical issues related to the use of placebo in clinical trials. *Hong Kong Medicine Journal*, 9(3):192-197.

Laub, M. 2008. Low back pain – anatomy, physiopathology and differential diagnoses (online). Available at http://www.123chiropractors.com/articles/lower-back-pain-anatomy-physiopathology-and-differential-diagnoses. [Accessed on 3 July 2014.]

Laurent, A., Mistretta, F., Bottigioli, D., Dahel, K., Goujan, C. and Nicolas, J. 2007. Echographic measurement of skin thickness in adults by high frequency ultrasound to assess the appropriate microneedle length for intradermal delivery of vaccines. *Vaccine,* 25:6423-6425.

Lawrence, T. 2009. The nuclear factor NF-KB pathway in inflammation. *Cold spring harbour perspectives in biology*, 1(6):1-10.

Leveille, S.G., Gurainik, J.M., Hochberg, M., Hirsch, R., Ferrucci, L., Langlois, J., Rantanen, T and Ling, S.1999.Low back pain and disability in older women: independent association with difficulty but not inability to perform daily activity.*Journal of genetology*.53(10):487-493

Levin, K.H.2000. Low Back Pain (online) Available at http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/neurology/low-back-pain/Default.htm [Accessed on 10 March 2015]

Liebenson, C. 2006. *Rehabilitation of the spine: a practitioner's manual*. 2nd ed. Baltimore: Lippincott, Williams and Wilkins

Liebenson, C. 2000. What is the mechanism of injury for low back pain? How is low back pain produced? *Dynamic chiropractic,* 18(9).

Lin, C., McAuley, J., Macedo, L., Barnett, D., Smeets, R. and Verbunt, J. 2011. Relationship between physical activity and disability in low back pain: a systematic review and meta-analysis. *Pain*, 152:607-613.

Liu, Y., Ye, X., Feng, X., Zhou, G., Rong,Z., Fang, C. and Chen, H. 2005. Menthol facilitates the skin analgesic effect of Tetracaine gel. *International journal of pharmaceutics,* 305:31-36.

Long, A., Donelson, R. and Fung, T. 2004. Does it matter which exercise? a randomized controlled trial of exercise for low back pain. *Spine*. 29(23):2593-2602.

Lynch, S. 2002. Assessment of the injured ankle in the athlete. *Journal of athletic training*, 37(4):406-412.

Lyss, G., Schmidt, J., Merfort, I. and Paul, H.L. 1998. Helenali, an anti-inflammatory sesquiterpene lactone from Arnica, selectively inhibits transcription factor NF-KB. *Biological chemistry*, 378:951-961.

Maigne, J.Y. and Vautravers, P. 2003. Mechanism of action of spinal manipulative therapy. *Joint bone spine*, 70:336.

MacPherson, L.J., Hwang, S.W., Miyamoto, T., Dubin, A.E., Pataputian, A. and Story, G.M. 2006. More than cool: promiscuous relationships of menthol and other sensory compunds. *Molecular and cellular neouroscience*, 32:335-343.

Malanga, G. 2011. Lumbosacral facet syndrome (online). Available at: http://emedicine.medscape.com/article/94871-overview. [Accessed date 3 July 2014.]

Mannion, A., Balagué, F., Pellisé, F. and Cedraschi, C. 2007. Pain measurements in patients with low back pain*. Nature clinical practice rheumatology*, 3:610-618.

Margetts, L and Sawyer, R.2007.Transdermal drug delivery:principles and opiod therapy. Continuing education in anaesthesia, critical care an pain.7:171-175

Martin, D., Valdez, J., Boren, J and Mayersohn, M.2004. Dermal absorption of camphor, menthol and methyl salicylate in humans. *Clinical Pharmacology.*44:1151-1157

McKemy, D.D., Neuhausser, W.M. and Julius, D. 2002. Identification of cold receptor reveals a general role for TRP channels in thermosensation. *Nature* 416(6876):52-57.

McMurray, M. 2011. The soft tissue structures of the lumbar spine. *The journal of the spinal research foundation*, 6(1).

McMurrich, J.P and Sobatta, J.2000.*Atlas and text book of human anatomy-vascular system, lymphatic system, nervous system and sense organs*. *Volume 3*.Moscow:Ripol Klassick.p60-61

Melzack, R. and Wall, P. 1965. Pain mechanisms: a new theory. *Science,* 150(3699):971-979.

Meissner, K., Kohls, N and Colloca, L. 2010. Introduction to the placebo effect in medicine: mechanisms and clinical implications. *Philosophical transactions of the royal society*, 366:1783-1789.

Merrick, M.A., Jutter, L.S. and Smith, M.E. 2003. Cold modalities with different thermodynamic properties produce different surface and intramuscular temperatures. *Journal of athletic training,* 38(1):28-33.

Mirtz, T.A., Greene, L. 2005. Is obesity a risk factor for low back pain? an example of using the evidence to answer a clinical question. *Chiropractic & osteopathy*,13(2):1340-1346.

Montgomery, G.H. and Kirsch, I. 1996. Classical conditioning and the placebo effect. *Pain*, (72):107-113.

Monticone, M., Baiordi, P., Vanti, C., Ferrari, S., Pillastrini, P., Mugnai, P and Foti, C.2012.Responsiveness of the Osweatry Disability Index and the Roland Morris Disability Quationnaire in Italian subjects with sub-acute and chronic low back pain. *European spine journal*.21(1)122-129

Moody, M.L. 2010. Topical medications in the treatment of pain. *Pain medicine news*, p15-20.

Moore, K. and Dalley, A. 2005. *Clinically orientated anatomy*. 5th ed. Philadelphia: Lippincott, Williams and Wilkins. p538-540 and p357-358.

Morgan, A. 2012. Cryotherapy (online). Available at: emedicine.medscape.com/article/112585. [Accessed on 30 October 2014.]

Moroder, P., Runer, A., Resch, H. and Tauber, M. 2011. Low back pain among medical students. *Acta Orthopaedica Belgica,* 77(1):88-92.

Morris, C. 2006. *Low back pain syndromes: integrated clinical management*. New York: The McGraw Companies

Morrow, D. 2014. Debunking acute low back pain (online). Available at http://www.prairiespine.com/spine-care/debunking-acute-low-back-pain/. [Accessed on 30 October 2014.]

Nadler, S., Weingand, K., Kruse, R.J. 2004. The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner*. Pain physician,* 7(3):395-397.

Naish, J., Revest, P. and Court, D. 2009. *Medical sciences*. London: Elsevier.

Nallamothu, B.K., Haywards, R.A. and Bates, C.R. 2008. Beyond the randomised clinical trial: the role of effectiveness in studies in the evaluation of cardiovascular therapies. *Circulation*, 118:1295-1303.

Nestor, K. and Sheidler, K. 2008. Sacroilliac joint (online). Available at: http://www.physio-pedia.com/Sacroiliac_joint. [Accessed date 30 June 2014.]

Nussbaum, E.L. and Downes, L. 1998. Reliability of clinical pressure-pain algometric measurements obtained on consecutive days. *Physical therapy*, 78:161.

Nyland, L.J. and Grimmer, K.A. 2003. Is undergraduate physiotherapy study a risk factor for low back pain? a prevalence study of LBP in physiotherapy students. *BMC musculoskeletal disorders,* (4):22.

Ostelo, R. and de Vet, H. 2005. Clinically important outcomes in low back pain. *Best practice and research clinical rheumatology,* 19(4):593-607.

Page, P. and Mackison, D. 2007. New alternatives to pain medication: how natural pain relievers can help (online). Available at: http://www.toyourhealth.com/mpacms/tyh/article.php?id=8. [Accessed on 26 November 2014.]

Patel, A.T. and Ogle, A.A. 2000. Diagnosis and management of acute low back pain. *American family physician*, 61(6):1779-1786.

Patel, T., Ishiuji, Y. and Yoshipovitch, G. 2007. Menthol: a refreshing look at an old compound. *Journal of American academy of dermatology,* 57(5):873-878.

Peier, A.M., Moqrich, A., Hergarden, A.C., Reeve, A.J., Andersson, D.A., Story, G.M., Earley, T.J., Dragoni, I., McIntyre, P., Bevan, S. and Patapoutian, A. 2002. A TRP channel that senses cold stimuli and menthol. *Cell,* 108(5):705-715.

Peiser, L. and Gordon, S. 2009. Phagocytosis: enhancement (online). Available at: http://onlinelibrary.wiley.com/doi/10.1002/9780470015902.a0001214.pub2/full. [Accessed date 15 August 2014.]

Petrovic, P., Kalso, E., Petersson, K. and Ingvar, M. 2002. Placebo and opiod

analgesia-imaging a shared neuronal network. *Science*, 295:1737-1740.

Plesh, O., Adams, S. and Gansky, S. 2011. Racial/ ethnic and gender prevelances in reported common pains in a national sample. *Journal of orofacial pain*, 25(1):25-31.

Pottera, L., McCarthy, C. and Oldhama, J. 2006. Algometer reliability in measuring pressure pain threshold over normal spinal muscles to allow quantification of anti-nociceptive treatment effects. *International journal of osteopathic medicine*, 9(4):113-119.

Prentice, W. 2011. *Therapeutic modalities in rehabilitation*. 4th ed. New York: McGraw-Hill Medical.

Purves, D., Augustine, G.J. and Fitzpatrick, D. 2001. *Neuroscience.* "Mechanoreceptors specialized to receive tactile information." Sunderland, MA: Sinauer Associates, Inc. p1-2.

Quinn, E. 2014. RICE is bBest for soft tissue injuries (online). Available at: http://sportsmedicine.about.com/cs/rehab/a/rice.htm. [Accessed on 16 October 2014.]

Rajagopal, S. 2006. The placebo effect. *Psychiatric bulletin*, 30:185-188.

Reddi, D., Churran, N. and Stephens, R. 2013. An introduction to pain pathways and mechanisms. *British journal of hospital medicine*, 74(12):C188.

Richards, R. 2011. The pain-spasm-pain cycle (online). Available at: http://www.rachel-richards.com/news-may2011.php. [Accessed on 19 November 2014.]

Ricciotti, E. and FitzGerald, G.A. 2011. Prostaglandins and inflammation. *Arterioscleriosis, thrombosis, and vascular biology*, 31(5):986-1000.

Rinniger, J.A., Kickner, S., Chigurupati, P., McLean, A. and Franck, Z. 2000.

Immunopharmacological activity of Echinacea preparations following simulated digestion on murine macrophages and human peripheral blood mononuclear cells. *Journal of leukocyte biology*. 68:503-509.

Rippey, J.J. 2006. *General pathology: illustrated lecture notes*. Cape Town: Juta.

Roelofs, P.D., Deyo, R.A., Koes, B.W., Scholten, R.J. and van Tulder, M.W. 2008. Non-steroidal anti-inflammatory drugs for low back pain. *Cochrane Database Systematic Review.*

Rogers, N. and Rowland, K. 2011. An alternative to oral non-steroidal anti-inflammatory drugs for musculoskeletal injuries. *Journal of family practice,* 60(3):147.

Roland, M. and Fairbank, J. 2000. Roland Morris Disability Questionnaire and the Oswestry Disability Questionnaire. *Spine,* 24:3115-3124.

Roland, M. and Morris.1983. A study of the natural history of low back pain: part 1. Development of a reliable and sensitive measure of disability in low back pain. *Spine*, 8:141-4.

Rutherford, B.R., Wager, T.D. and Roose, S.P. 2010. Expectancy effects in the treatment of depression: a review of experimental methodology, effects on patient outcome and neural mechanisms. *Current reviews in psychiatry*, 6:1-10.

Saeki, Y.2002.Effect of the local application of cold or heat for relief of pricking pain.*Nursing health science*.4:97-105

Sakamaki, S., Yasushara, Y., Motoki, K., Takase, K., Tanioka, T. and Locsin, R. 2013.The relationship between BMI, thickness in subcutaneous fat and the gluteus muscle as the intramuscular injection site. *Health,* 5(9):1443-1448.

Satam, S., Jain, R., Dagaonkar, J., Chotalia, C., Suthar, A. and Joshi, R. 2011. Clinical study to establish efficacy and safety of Contodol gel as topical pain relieving agent. *Pharmacologyonline,* 1:765-771.

Sawynok, J.2003.Tropically and peripherally acting analgesics.*Pharmacological reviews,* 55(1):1-20

Schiphorst-Preuper, H.R., Reneman, M.F., Boonstra, A.M., Dijikstra, P.U., Versteegen,G.J., Geertzen, J.H.B. and Brouwer, S. 2008. Relationship between psychological factors and performance based and self-reported disability in chronic low back pain. *European spine journal,* 17(11):1448-1456.

Shankar, H., Scarlett, J.A. and Abram, S.E. 2009. Anatomy and pathophysiology of intevertebral disc disease. *Techniques in regional anaesthesia and pain management*, 13:67-75.

Sheps, S.G. 2014. Doppler ultrasound: what is it used for ?(online). Available at: http://www.mayoclinic.org/doppler-ultrasound/expert-answers/faq-20058452. [Accessed date 31 October 2014.]

Sherman, A.L. 2014. Sacroilliac joint injury (online). Available at: http://emedicine.medscape.com/article/96054-overview. [Accessed date 18 November 2014.]

Shiel, W. 2014. Low back pain (online). Available at: http://www.medicinenet.com/script/main/art.asp?articlekey=289. [Accessed date 30 August 2014.]

Shiri, R., Karppinen, J., Leino-Arjas, P., Solovieva, S., Vilkari-Juntura, E. 2009. The association between obesity and low back pain: a meta-analysis. *American journal of epidemiology*, 171(2):135-154.

Shulz, K and Grimes, D. 2002. Blinding in randomised clinical trials: hiding who got what*. Lancet*, 359:696-700.

Simons, D., Travell, J. and Simons, L. 1999. *Travell and Simons' myofascial pain and dysfunction: the trigger point manual. Volume one: upper half of the body.* 2nd

edition. Baltimore: Williams and Wilkins. p130-133.

Speroni, E., Govan, P., Guizzardi, S., Renzulli, C. and Guerra, M.C. 2002. Anti-inflammatory and cicatrizing activity of *Echinacea Pallida Nutt* root extract. *Journal of Ethnopharmacology*, 79:265-272.

Starkey, C.2013.*Therapeutic Modalities*.4th edition.United States of America: F.A Davis Company.p144

Standring, S. 2008. *Gray's anatomy: the anatomical basis of clinical practice*. 40th ed. Edinburgh: Elsevier Health Sciences.

Stedman, T.L. 2005. *Medical dictionary for health professionals and nursing*. Baltimore: Lippincott, Williams and Wilkins

Stenberg, G. and Ahlgren, C. 2010. A gender perspective on physiotherapy treatment in patients with neck and back pain. *Advances in physiotherapy,* 12(1):35-41.

Stewart-Williams, S. and Podd, J. 2004. The placebo effect: dissolving the expectancy versus conditioning debate. *Physiological bulletin*, 130(2):324-340.

Swenson, C., Sward, L. and Karlson, J. 1996. Cryotherapy in sports medicine. *Scandinavian journal of medical science and sports*, 6(4):193-200.

Tadicherla, S. and Berman, B. 2006. Percutaneous dermal drug delivery for local pain control. *Therapeutic clinical risk management,* 2(1):99-113.

Tanaka, T., Leisman, G., Mori, H. and Nishijo, K. 2002. The effect of massage on localised lumbar muscle fatigue. *BMC complementary and alternative medicine,* 2(9).

Tobin, D., Shaw, T. and Daly, W. 2009. Obesity and low back pain: a review of the literature. The greater Glasgow back pain scale (unpublished).

Topp, R., Winchester, L., Mink, A., Kaufman, J. and Jacks, D. 2011. Comparison of the effects of ice and 3.5% menthol gel on blood flow and muscle strength of the lower arm. *Journal of sport rehabilitation,* 20:355-366.

Tsuzuki, K., Xing, H., Ling, J. and Gu, J.G. 2004. Menthol induced calcium ion release from pre-synaptic calcium ion stores potentiates sensory synaptic transmission. *Journal of neuroscience,* 24(3)762-771.

Van Tulder, M.W., Becker, A., Bekkering, T., Breen, A., del Real, M.T., Hutchinson, A., Koes, B., Laerum, E. and Malmivaara, A. 2006. European guidelines for management of acute non-specific low back pain in primary care. *European spine journal,* 15:169-191.

Van Tulder, M.W., Touray, T., Furlan, A.D., Solway, S. and Bouter, L.M. 2003. Muscle relaxants for non-specific low back pain: a systematic review within the framework of the Cochrane Collaboration. *Spine*, 28:1978-1992.

Viester, L., Verhagen, E., Hengel, K., Koppes, L., van der Beek, A. and Bongers, P. 2013. The relation between body mass index and musculoskeletal symptoms in the working population. *BMC musculoskeletal disorders*, 14:238.

Vignoli, R. 2011. The muscle pain and spasm cycle (online). Available at: https://sites.google.com/site/massagebruxellesadomicile/articles-interessants/themusclepainandspasmcycle. [Accessed on 16 August 2014.]

Villarreal, G., Zagorski, J. and Wahl, S.M. 2001. *Encyclopedia of life sciences.* “Inflammation: acute.” London: Nature Publishing Group.

Vleeming, A., Mens, J., de Vries, H., van Wingerden, J.P. and Pool, A. 1998. The possible role of the long dorsal sacro-illiac ligament in peripartum pelvic pain. 3rd interdisciplinary world congress on low back pain and pelvic pain. p149

Wagner, S., Suter, A. and Merfort, I. 2004. Skin penetration studies of arnica

preparation and of their sesquiterpene lactons. *Plantation medicine*, 70:897-803.

Walker, J. 2012. Back pain: pathogenesis, diagnosis and management. *Nursing standard*, 27(14):49-56.

Wassung, K. 2012. The role of inflammation in the healing process (online). Available at: http://cichirowc.com/uploads/2012-01-30_Inflammation_and_the_healing_process.pdf. [Accessed date 27 July 2014.]

Wasner, G., Schattschneider, J., Binder, A. and Baron, R. 2004. Topical menthol: a human model for cold pain by activation and sensitization of C nociceptors. *Brain,* 127:1159-1171.

Weber, K. 2009. The technical benefits of icing (online). Available at: http://www.gomoji.com/blog/technical-benefits-icing/. [Accessed date 27 July 2014.]

Wright, A. and Sluka, K. 2001. Non-pharmalogical treatment for musculoskeletal pain. *Clinical journal of pain*, 17(1):33-46.

Wolfe, M.W., Uhl, T.L. and Mc Cluskey, L. C.2001. Management of ankle sprains. *American family physician*, 63(1):93.

Woznicki, K. 2014. What's your pain tolerance?(online). Available at: http://www.webmd.com/pain-management/features/whats-your-pain-tolerance. [Accessed date 22 October 2014.]

Ylinen, J., Nykanen, M., Kautiainen, H. and Haikkinen, A. 2007. Evaluation of repeatability of pressure algometer of neck muscles for clinical use. *Manual therapy,* 12:192-197.

Zhang, J., Enix, D., Snyder, B., Giggey, K. and Tepe, R. 2008. Effects of Biofreeze® and chiropractic adjustments on acute low back pain: a pilot study. *Journal of chiropractic medicine*, 7:59-65.

Zubieta, J., Bueller, J., Jackson, L., Scott, S., Xu, Y., Koeppe, R. and Stohler, C. 2005. Placebo effects mediated by endogenous opioid neurotransmission and opioid receptors. *Journal of neuroscience*, 25:7754-7762.

APPENDIXES

Appendix A: Ligaments of the low back region

Table A.1: The ligaments of the low back region

Ligament	Proximal Attachment	Distal Attachment	Function	Innervation
Anterior Longitudinal (ALL)	A broad ligament, beginning at the occiput which attaches to the anterior surface of the vertebral bodies and the intervertebral disc (IVDs)	The ALL runs along the entire length of the spine into the sacral region.	Limits extension and maintains the stability of the joints.	Splanchnic nerve
Posterior Longitudinal (PLL)	A narrow band that attaches to the posterior aspect of the vertebral bodies. It is widened over the IVDs and appears narrow over the vertebral bodies		Resists excessive flexion and distraction of the lumbar spine .	Sinuvertebral nerve
Suprapinous	The tip of the spinous process of the vertebra above.	The tip of the spinous process of the vertebra below.	Weakly limits flexion of the lumbar spine.	Medial branch of the dorsal rami
Interspinous	Root of the spinous process.	Apex of the spinous process, filling the anterior to posterior length of the spinous process.	Limits the end range of lumbar flexion.	
Ligamentum Flavum	A broad attachment to the inferior surface of the superior lamina.	Superior edge of the inferior lamina.	It is normally a taut ligament, stretching for flexion and contracting its fibre during a neutral position or extension.	
Intertansverse	A ligament that runs the entire length of the spine attaching to the inferior aspect of the superior transverse process	Superior aspect of the transverse process below	Resists lateral bending of the lumbar spine.	
Iliolumbar	Transverse processes of L5	Ipsilateral side of the sacrum and the inner lip of the iliac crest.	It assists in stabilization of the lumbosacral joints and resists forward sliding of L5 on the sacrum. Unilaterally, it acts to resist side bending, forward bending and excessive rotational movement.	Ventral and dorsal rami of L4 an L5
Interosseous	Sacral fossae	Ipsilateral ischial	Resists anterior and inferior movement of	Dorsal root

Sacroilliac(SI)		tuberosity.	the sacrum.	ganglia of L4-S2
Anterior SI	Pelvic surface of the SI joint.	Fibrous articular capsule of the SI joint.	Provides structural support for the SI joint.	Dorsal root ganglia of L1-S2
Posterior SI	Long posterior SI ligament Posterior inferior iliac spine (PSIS) Short posterior SI ligament The intermediate and lateral sacral crests at S1 and S2 and runs in a horizontal plane, covering the SI joint posteriorly.	Long posterior SI ligament Lateral sacral crests of S3 and S4 and some fibres blend with the sacrotuberous ligament Short posterior SI ligament The medial aspect of the posterior surface of the iliac crest and iliac tuberosity.	Both parts of the ligament are found to be tense during the transmission of forces from the lower limb to the thorax and vice versa, thus the ligament acts as a shock absorber. The posterior SI ligament has also been noted to be tense during counter-nutation, posterior rocking of the sacrum and slack during nutation of the sacrum, the opposite is true for the sacrotuberous ligament. Thus a complex is set up between the posterior SI ligament and the sacrotuberous ligament to provide stabilization to the sacrum.	Dorsal root ganglia of L4-S2
Sacrotuberous	The PSIS, the posterior aspect of the long posterior SI ligament, the inferior aspect of the lateral sacral crest , and the lateral edge of the inferior sacrum and the lateral coccyx	The medial aspect of the ischial tuberosity	Works in conjunction with the sacrospinous ligament.	Dorsal root ganglia of L4-S2
Sacrospinous	The anterior surface of the sacrum	The ischial spine	Together with the sacrotuberous ligament, these ligaments will assist in stabilizing the inferior aspect of the SI joint and limiting the amount of anterior and inferior nutational (anterior rocking of the sacral base) or nodding movement of the sacrum at the SI joint. This is accomplished by restricting the movement of the sacral apex from excessive posterior and superior movement, when the	Dorsal root ganglia of L1-S2

			anteriorly located promontory of the sacrum, moves anterior and inferior.	

(Vleeming, 1998; Higuchi and Sato, 2002; Bogduk, 2005; Nestor and Sheidler, 2008; Moore and Dalley, 2010; Higgins, 2011, McMurray, 2011; Cramer and Darby, 2014; Kishner, 2014).

Appendix B: Extrinsic muscles of the lower back area

Table B.1: The extrinsic muscles of the lower back area

LatissimusDorsi	Spinous processes of T7-T12, thoracolumbar fascia,iliac crest and the inferior 3rd to 4th ribs.	Intertubecular groove of the humerus	Thoracodorsal nerve (C6-C8)	Extends, adducts and medially rotates the humerus and raises the body toward the arms during climbing.
QuadratusLumborum	Medial half of the inferior of 12th ribs and tips of the lumbar transverse processes	Iliolumbar ligament and internal lip of the iliac crest	Anterior branches of the T12 and L1 – L4 nerves	Extends and laterally flexes the vertebral column and fixes the 12th rib during inspiration,
Gluteus maximus	Posterior ilium, posterior glureal line, posterior surface of the sacrum and coccyx and the sacrotuberousligament	Some fibres insert into the iliotibial tract, which inserts into the lateral condyle of the tibia and some fibres attached into the gluteal tuberosity.	Inferior gluteal nerve	Extends, laterally rotates the thigh and assists in rising from the sitting position.
Gluteus medius	External surface of the ilium between the anterior and posterior gluteal lines	Lateral surface of the greater trochanter of the femur	Superior gluteal nerve	Abducts and medially rotates the thigh, keeps the pelvis level when the ipsilateral limb is weight bearing and advances the opposite limb(unsupported) during the swing phase of the gait cycle.
Gluteus minimus	External surface of the ilium between the anterior and inferior gluteal lines	Anterior surface of the greater trochanter of the femur	Superior gluteal nerve	

(Moore and Dalley, 2005)

Table B.2: The intrinsic muscles of the lower back area (intermediate layer)

Muscle	Origin	Insertion	Nerve Supply	Main Action
Erector Spinae **Iliocostalis** **Longissimus** **Spinalis**	A broad tendon for the posterior of the iliac crest, posterior of the sacrum,sacroilliac ligaments, the lumbar and sacral spinous processes and the supraspinous ligament	Iliocostalis: lumbar and thoracic fibres run superiorly to the angles of the lower ribs and cervical fibres sun to the cervical transverse processes. Longissimus:thoracic and cervical fibres run superiorly to the	Posterior rami of the spinal nerves	Bilaterally :extends the vertebral coloumn and the head; when the back is flexed- it controls movement by lengthening. Unilaterally: lateral flexion of

		ribs, between the tubercle and the angle, to the transverse processes in the thoracic and cervical regions . The capitis fibres sun towards the mastoid process of the temporal bone. Spinalis:thoracis and cervical fibres run superiorly towards the spinous processes in the upper thoracic region and to the cranium		the vertebral coloumn

(Moore and Dalley, 2005)

Table B.3: The intrinsic muscles of the lumbosacral area (deep layer)

Muscle	Origin	Insertion	Nerve Supply	Main Action
Transversospinal **Semispinalis** **Multifidus** **Rotatores**	Semispinalis : C4-T12 transverse processes Multifidus:posteriorsacrum,posterior superior iliac spine of the the ilium, aponeurosis of erector spinae, sacroilliac ligaments, lumbar mammillary processes, T1-T3 transverse processes and the C4-C7 articular processes Rotatores:transverse processes of the vertebrae	Semispinalis: thoracic, cervical and capitis fibres run superomedially to the occipital bone and the spinous processes in thoracic and cervical regions spanning 4-6 segments Multifidus: fibres pass superomedially to the entire length of spinous processes of the vertebrae, located 2-4 segments superior to the origin Rotatores: fibres passsuperomedially to attach the the junction of the lamina and transverse processes or spinous processes of vertebrae immediately(brevis)or 2 segments superior to vertebrae of origin (longus).	Posterior rami of the spinal nerves	Semispinalis: Extends and contralaterally rotates the head, thoracic and cervical regions. Multifidus: stabilizes the vertebrae during local movements of the vertebral column Rotatores: stabilize vertebrae and assist with local extension and rotatory movements of the vertebral column.
Interspinalis	Superior surfaces of the cervical	Inferior surfaces of	Posterior	Extension and

	and lumbar spinous processes	spinous processes of the vertebra superior to the vertebrae of origin.	rami of the spinal nerves	rotation of the vertebral column
Intertransversarii	Cervical and lumbar vertebrae transverse processes	Transverse processes of adjacent vertebrae	Anterior and posterior rami of the spinal nerves	Lateral flexion of the vertebral coloumn when acting unilaterally and bilaterally, stabilizes the vertebral column.

(Moore and Dalley 2005)

Appendix C: Durban University of Technology

Institutional Research Ethics Committee approval

DUT
DURBAN
UNIVERSITY OF
TECHNOLOGY

Institutional Research Ethics Committee
Faculty of Health Sciences
Room MS 49, Mansfield School Site
Gate 6, Ritson Campus
Durban University of Technology

P O Box 1334, Durban, South Africa, 4001

Tel: 031 373 2900
Fax: 031 373 2407
Email: lavishad@dut.ac.za
http://www.dut.ac.za/research/institutional_research_ethics

www.dut.ac.za

6 February 2014

IREC Reference Number: **REC 81/13**

Ms C K Prince
Flat 11 Raylene
60 Ritson Road
Berea
Durban
4001

Dear Ms Prince

The effect of three different cooling gels on acute non-specific low back pain

I am pleased to inform you that Full Approval has been granted to your proposal REC 81/13. You are requested to ensure the following:

- All telephonic interviews are to be recorded and stored as part of the documentation.

The Proposal has been allocated the following Ethical Clearance number IREC 006/14. Please use this number in all communication with this office.

Approval has been granted for a period of one year, before the expiry of which you are required to apply for safety monitoring and annual recertification. Please use the Safety Monitoring and Annual Recertification Report form which can be found in the Standard Operating Procedures [SOP's] of the IREC. This form must be submitted to the IREC at least 3 months before the ethics approval for the study expires.

Any adverse events [serious or minor] which occur in connection with this study and/or which may alter its ethical consideration must be reported to the IREC according to the IREC SOP's. In addition, you will be responsible to ensure gatekeeper permission.

Please note that any deviations from the approved proposal require the approval of the IREC as outlined in the IREC SOP's.

Yours Sincerely

[redacted]

Prof J K Adam
Chairperson: IREC

Appendix D: Advert

low back pain of approximately 1 week???

IF YOU ARE BETWEEN THE AGES OF 18 AND 40

YOU COULD BE ELIGABLE TO PARTICIPATE IN MY STUDY!

IF YOU ARE INTERESTED CONTACT

CLEO

OR

THE CHIROPRACTIC DAY CLINIC, DURBAN UNIVERSITY OF TECHNOLOGY031 373 2205

Appendix E: Permission to place advertisement on premises

To whom it may concern

I am currently conducting a research trial, at the Durban University of Technology at the Chiropractic Day Clinic, involving the recruitment of 60 male or female participants, between the ages of 18 and 40. The recruitment of these participants requires advertising using the attached advertisement.

Your permission to allow for these advertisements to be placed on your premises will be greatly appreciated.

Kind Regards

Cleo Prince

Student Number 20807313

Appendix F: Permission to use Chiropractic Day Clinic

MEMORANDUM

To : Prof Puckree

Chair : RHDC

Prof Adam

Chair : IREC

From : Dr Charmaine Korporaal

Clinic Director : Chiropractic Day Clinic : Chiropractic and Somatology

Date : 27.07.2013

Re : Request for permission to use the Chiropractic Day Clinic for research purposes

Permission is hereby granted to :

Ms Cleo Prince (Student Number: 20807313)

Research title : The effect of three different cooling gels on acute non-specific low back pain

It is requested that Ms Prince submit a copy of her RHDC / IREC approved proposal to the Clinic

Administrators before she starts with her research in order that any special procedures with regards to

her research can be implemented prior to the commencement of her seeing patients.

Thank you for your time.

Kind regards

Dr Charmaine Korporaal

Clinic Director : Chiropractic Day Clinic : Chiropractic and Somatology

Cc: Mrs Pat van den Berg : Chiropractic Day Clinic

Dr L O'Connor : Research co- ordinator and research supervisor

Appendix G: Letter of Information and Informed Consent

Letter of Information and Consent

Dear Participant

Thank you for volunteering your time to be part of my study. I am currently completing my MTech : Chiropractic qualification at the Durban University of Technology**.**

Title of the Research Study:

The effect of three different cooling gels on acute non-specific low back pain

Researcher: Cleo Prince, B. Tech: Chiropractic

Supervisor/s: Dr. Laura O' Connor (supervisor), M. Tech: Chiropractic, CCEP
Prof. David Gerber (co-supervisor),BVSc, PhD

Back ground to the study: Low back pain is a common complaint that is treated by chiropractors and other manual therapist. Today many practitioners use cooling gels to apply cold therapy rather than traditional ice packs, the reason for this is that there is no need for refrigeration and the cooling gels are easily accessible. However there is little information available to determine which, out of three cooling gels is effective in treating acute low back pain. Therefore this study is investigating the effectiveness of a menthol cooling gel with anti-inflammatory herbs, menthol based gel and a placebo gel in the treatment of acute non-specific low back pain.

Outline of the Procedures:

The first consultation will take place at the Chiropractic Clinic at the Durban University of Technology and will take approximately two and a half hours. You will be given a verbal explanation of the study, thereafter you will be required to read and sign this letter of information and consent. You will then have a case history, physical and lumbar spine (low back) examination. A small mark of henna will be made on a certain point on your low back, this point will be used as a marker to ensure that the researcher assess the exact same point at the follow up consultations. The examination will aid in determining your eligibility to participate in the study. Should you be eligible you will be randomly allocated to one of three groups, groups will receive the menthol based cooling gel with anti – inflammatory herbs, menthol based cooling gel or a placebo gel, there is a 33% chance that you will be in the group receiving the placebo gel. You will be given a tub of gel and a tablespoon to be utilized for your home applications. The researcher will then rub a tablespoon of the gel onto your lower back. You will be required to take the gel home and to apply a level tablespoon to your lower back area, between the rib cage and the buttocks, no more than three times a day rubbing the gel in for approximately 30 seconds to allow the gel to be absorbed by the skin. The duration of this study is one week, and you will be required to attend two follow up consultations, which will each be an hour long.

Benefit:

The study will be beneficial to manual therapists such as chiropractors to determine a more effective management plan for acute low back pain

Risks/Discomforts to the Subject and Product info:

In previous studies utilizing the same gel, to be used in this study, no adverse reactions were reported from gel use. However should you develop any adverse reactions, please stop using the gel and inform the researcher immediately. The menthol cooling gel was found to be non-irritant however should you develop any skin irritation or dryness please discontinue using the gel immediately, wash the area with water and contact the researcher or the supervisor. Do not use the gels in this study over open wounds or sensitive skin. Avoid exposure to the eyes and use the gels for external use only.

Reason/s why the Participant May Be Withdrawn from the Study:

You are free to withdraw at any time and it will not affect future treatments at the chiropractic clinic should you wish to return.

Remuneration:

By participating in this study there will be no cost to you nor will you receive any remuneration except for the free treatment.

Confidentiality:

Confidentiality will be maintained as only the researcher and supervisor will have access to the patient files, and in the dissertation no personal information will be disclosed only the demographics and results of each group will be discussed.

Research-related Injury:

Should you develop any side effects from participating in the research, please inform the researcher immediately. You will then be examined by the researcher and if necessary referred appropriately.

Persons to Contact in the Event of Any Problems or Queries:
Should you have any queries, feel free to contact the researcher (Cleo Prince) or 031 373 2205.If the researcher cannot be contacted please contact the supervisor,Dr. O'Connor on 031 3732923 or the Institutional Research Ethics administrator on 031 373 2900. Complaints can be reported to the DVC: TIP, Prof F. Otieno on 031 373 2382 or dvctip@dut.ac.za.

CONSENT

Statement of Agreement to Participate in the Research Study:
I hereby confirm that I have been informed by the researcher, Cleo Prince, about the nature, conduct, benefits and risks of this study - Research Ethics Clearance Number: 006/14,

I have also received, read and understood the above written information (Participant Letter of Information) regarding the study.

I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.

In view of the requirements of research, I agree that the data collected during this study can be processed in a computerized system by the researcher.

I may, at any stage, without prejudice, withdraw my consent and participation in the study. I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.

I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

_____ _____ _____ _____
Full Name of Participant **Date** **Time** **Signature / Right Thumbprint**

I, Cleo Prince herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____ _____ _____

Full Name of Researcher **Date** **Signature**

_____ _____ _____

Full Name of Witness **Date** **Signature**

Appendix H:Case history

CHIROPRACTIC PROGRAMME

CHIROPRACTIC DAY CLINIC
CASE HISTORY

Patient:_____ Date: _____

File #:_____ Age: _____

Sex: _____ Occupation: _____

Student: _____ Signature _____

FOR CLINICIANS USE ONLY:

Initial visit

Case History:

Examination:

Previous: Current:

X-Ray Studies:

Previous: Current:

Clinical Path. lab:

Previous: Current:

CASE STATUS:

PTT:	Signature:	Date:

CONDITIONAL:

Reason for Conditional:

.....

.....

.....

.....

Conditions met in visit no:	Signed into PTT:	Date:

Case Summary signed off:	Date:

2. Chief Complaint: (patient's own words):

3. Present Illness:

	Complaint 1(principle complaint)	**Complaint 2 (additional or secondary complaint)**
Location Onset : Initial: Recent: Cause: Duration Frequency Pain (Character) Progression Aggravating Factors Relieving Factors Associated S & S Previous Occurrences Past Treatment Outcome:		

4. Other Complaints:

5. Past Medical History:

General Health Status

Childhood Illnesses

Adult Illnesses

Psychiatric Illnesses

Accidents/Injuries

Surgery

Hospitalizations

6. Current health status and life-style:

Allergies

Immunizations

Screening Tests incl. x-rays

Environmental Hazards (Home, School, Work)

Exercise and Leisure

Sleep Patterns

Diet

Current Medication

Analgesics/week:

Other (please list):

Tobacco

Alcohol

Social Drugs

7. Immediate Family Medical History:

Age of all family members
Health of all family members
Cause of Death of any family members

	Noted	Family Member		Noted	Family Member
Alcoholism			Headaches		
Anaemia			Heart Disease		
Arthritis			Kidney Disease		
CA			Mental Illness		
DM			Stroke		
Drug Addiction			Thyroid Disease		
Epilepsy			TB		
Other (list)					

8. Psychosocial history:

Home Situation and daily life
Important experiences
Religious Beliefs

9. Review of Systems (please highlight with an asterisk those areas that are a problem for the patient and require further investigation)

General

Skin

Head

Eyes

Ears

Nose/Sinuses

Mouth/Throat

Neck

Breasts

Respiratory

Cardiac

Gastro-intestinal

Urinary

Genital

Vascular

Musculoskeletal

Neurologic

Haematological

Endocrine

Psychiatri

CHIROPRACTIC PRGRAMME

PHYSICAL EXAMINATION:

SENIOR

Patient Name : _____ **File No:** _____ **Date:** _____

Student: _____ **Signature :**_____

VITALS:				
Pulse Rate:			Respiratory Rate:	
Blood Pressure:	R	L	Medication if hypertensive:	
Temperature			Height	
Weight:	Any recent change ?	Y/N	If yes: How much gain/loss	Over what period

GENERAL EXAMINATION:		
General Impression		
Skin		
Jaundice		
Pallor		
Clubbing		
Cyanosis		
Oedema		
Lymph Nodes	Head and Neck	
	Axillary	
	Epitrochlear	
	Inguinal	
Pulses		
Urinalysis		

SYSTEM SPECIFIC EXAMINATION:
CARDIOVASCULAR EXAMINATION
RESPIRATORY EXAMINATION
ABDOMINAL EXAMINATION
NEUROLOGICAL EXAMINATION
COMMENTS

Clinician: **Signature:**

Appendix J: Regional examination – lumbar spine and pelvis

CHIROPRACTIC PROGRAMME

REGIONAL EXAMINATION
LUMBAR SPINE AND PELVIS

Patient:_____ File#: _____ Date: _____

Student:_____ Clinician:_____

STANDING:

Posture– scoliosis, antalgia, kyphosis
Body Type
Skin
Scars
Discolouration

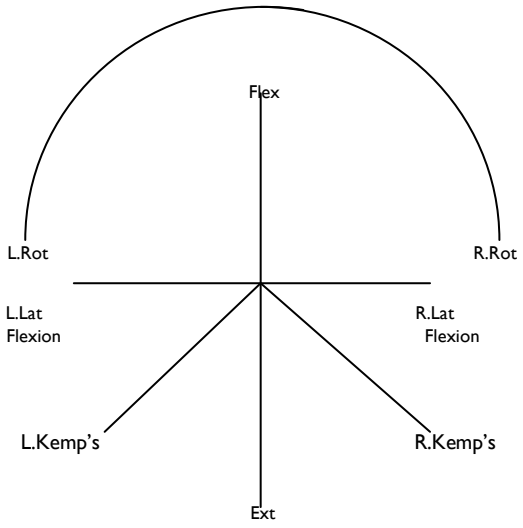
Minor's Sign
Muscle tone
Spinous Percussion
Schober's Test (6cm)
Bony and Soft Tissue Contours

GAIT:

Normal walking
Toe walking
Heel Walking
Half squat

ROM:

Forward Flexion = 40-60° (15 cm from floor)
Extension = 20-35°
L/R Rotation = 3-18°
L/R Lateral Flexion = 15-20°



Which movement reproduces the pain or is the worst?

- Location of pain
- Supported Adams: Relief? (SI)
- Aggravates? (disc, muscle strain)

SUPINE:

Observe abdomen (hair, skin, nails)
Palpate abdomen\groin
Pulses - abdominal
- lower extremity
Abdominal Reflexes

		Degree	LBP?	Location	Leg pain	Buttock	Thigh	Calf	Heel	Foot	Braggard
SLR	L										
	R										

	L	R
Bowstring		
Sciatic notch		
Circumference (thigh and calf)		
Leg length: actual -		
apparent –		
Patrick FABERE: pos\neg – location of pain?		
Gaenslen's Test		
Gluteus max stretch		
Piriformis test (hypertonicity?)		
Thomas test: hip \ psoas \ rectus femoris ?		
Psoas Test		

SITTING:

Spinous Percussion
Lhermitte

Valsalva

		Degree	LBP?	Location	Leg Pain	Buttock	Thigh	Calf	Heel	Foot	Braggard
TRIPOD **SI,+,++**	**L**										
	R										

SLUMP 7 TEST	**L**										
	R										

LATERAL RECUMBENT: **L** **R**

Ober's		
Femoral n stretch		
SI Compression		

PRONE : **L** **R**

Gluteal skyline		
Skin rolling		
Iliac crest compression		
Facet Joint Challenge		
SI tenderness		
SI Compression		
Erichson's		
Pheasant's		

MF tp's	**Latent**	**Active**	**Radiation**
QL			
Paraspinal			
Glut Max			
Glut Med			
Glut Min			
Piriformis			
Hamstring			
TFL			
Iliopsoas			
Rectus Abdominus			

NON ORGANIC SIGNS:

Pin point pain
Trunk rotation
Flip Test
Ankle dorsiflexion test
Axial compression
Burn's Bench test
Hoover's test
Repeat Pin point test

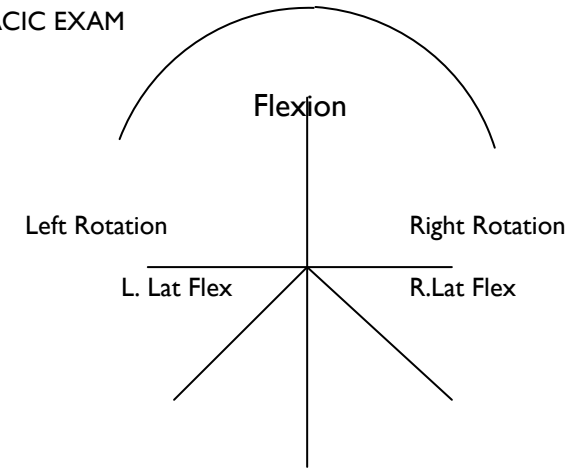
NEUROLOGICAL EXAMINATION

Fasiculations						
Plantar Reflex						
Level	Tender?	Dermatomes		DTR		
		L	R		L	R
T12				Patellar		
L1				Achilles		
L2						
L3				Proprioception		
L4						
L5						
S1						
S2						
S3						

Action	Muscles	Levels	L	R	
Lateral Flexion spine	Muscle QL				
Hip flexion	Psoas, Rectus femoris				5+ Full strength
Hip extension	Hamstring, glutes				4+ Weakness
Hip internal rotation	Glutmed, min, TFL, adductors				3+ Weak against grav
Hip external rotation	Gluteus max, Piriformis				2+ Weak w\o gravity
Hip abduction	TFL, Glut med and minimus				1+ Fascic w\o gross movt
Hip adduction	Adductors				0 No movement
Knee flexion	Hamstring,				
Knee extension	Quad				W-wasting
Ankle plantarflexion	Gastrocnemius, soleus				
Ankle dorsiflexion	Tibialis anterior				
Inversion	Tibialis anterior				
Eversion	Peroneus longus				
Great toe extensor	EHL				

BASIC THORACIC EXAM

Passive ROM



History: Left Kemp's Right Kemp's

BASIC HIP EXAM

History
ROM: Active
Passive: Medial rotation: A) Supine (neutral) If reduced
- hard \ soft end feel
B) Supine (hip flexed):

- Trochanteric bursa

MOTION PALPATION AND JOINT PLAY	L	R
Thoracic Spine		
Lumbar Spine		
Sacroiliac Joint		

Appendix K: Data collection sheet

Data Collection

Patient Name

.....

File Number ..... Group.....

Objective Measurements

	1st Visit - baseline	2nd Visit	3rd Visit
Algometer			

Subjective Measurements

	1st Visit - baseline	2nd Visit	3rd Visit
Numerical Pain Rating Scale			
Roland Morris Disability Index			

Appendix L: Numerical Pain Rating Score

Patient Name .....

Visit No. ☐

Numerical Pain Rating Score

0	1	2	3	4	5	6	7	8	9	10

Please indicate in the scale below the number between 0 and 10 that best describes your pain at this time. A zero (0) means 'no pain' and a ten (10) means 'the most severe pain'

Appendix M: Roland-Morris Disability Questionnaire

The Roland-Morris Disability Questionnaire

As you read the list, think of yourself *today*. When you read a sentence that describes you today, put a tick against it. If the sentence does not describe you, then leave the space blank and go on to the next one. Remember, only tick the sentence if you are sure it describes you today.

1. I stay at home most of the time because of my back.

2. I change position frequently to try and get my back comfortable.

3. I walk more slowly than usual because of my back.

4. Because of my back I am not doing any of the jobs that I usually do around the house.

5. Because of my back, I use a handrail to get upstairs.

6. Because of my back, I lie down to rest more often.

7. Because of my back, I have to hold on to something to get out of an easy chair.

8. Because of my back, I try to get other people to do things for me.

9. I get dressed more slowly then usual because of my back.

10. I only stand for short periods of time because of my back.

11. Because of my back, I try not to bend or kneel down.

12. I find it difficult to get out of a chair because of my back.

13. My back is painful almost all the time.

14. I find it difficult to turn over in bed because of my back.

15. My appetite is not very good because of my back pain.

16. I have trouble putting on my socks (or stockings) because of the pain in my back.

17. I only walk short distances because of my back.

18. I sleep less well because of my back.

19. Because of my back pain, I get dressed with help from someone else.

20. I sit down for most of the day because of my back.

21. I avoid heavy jobs around the house because of my back.

22. Because of my back pain, I am more irritable and bad tempered with people than usual.

23. Because of my back, I go upstairs more slowly than usual.

24. I stay in bed most of the time because of my back.

Appendix N: Agreement with clinic receptionist to assist in research

This is to certify that, I, in my capacity of the Chiropractic Clinic Receptionist, agree to assist the Researcher, Cleo Prince with her study. I acknowledge that the gels are to be kept at the clinic reception to ensure that the blinding process is adequate. If I am not available at the time to assist the researcher, another member of the admin staff has the permission to assist her.

Name of the Receptionist	**Signature**	**Date**
Name of the Researcher	**Signature**	**Date**

Appendix O: Memorandum of understanding between the researcher and HealthTech Laboratories

Durban University of Technology

Memorandum of understanding between:

The '**RESEARCH INSTITUTION**'- Durban University of Technology(this includes the respective research student and research supervisor, Department of Chiropractic. The Faculty of Health Sciences Research Committee, The Institutional Research Committee and any other related DUT employees.

AND

The '**MANUFACTURER**'- V-Tech (including all members, employees and associates).

The Memorandum of Understanding pertains to the following research project and must be read in conjunction with the following;

APPENDIX A – Detailed Research Proposal (PG4a)

APPENDIX B – Durban University of Technology Research Committee Research Ethics Policy and Guidelines

Title of the study: The effect of three different cooling gels on acute non-specific low back pain

Research Student: Cleo Prince, Student Number: 20807313

Research Supervisor: Dr Laura O' Connor (Department of Chiropractic and Somatology – Durban University of Technology)

This study is a Master's mini Dissertation conducted in partial compliance with the Master's Degree in Technology in the Department of Chiropractic- Faculty of Health Sciences- Durban University of Technology. This study will obtain ethical approval from the Faculty of Health Sciences Research and Ethics Committee (FRC) of the Durban University of Technology.

Section 1 – Funding of the study and Financial Commitment

1. A research allowance of R5000.00 has been awarded by the Dept. Post-graduate Development & Support –The details of the funds approved are described in Section A of the Research Proposal(PG4a) attached.

2. The ’MANUFACTURER’-will donate (free of charge) the respective experimental placebo gel and the cooling gel in quantities sufficient to meet the requirements described in the research proposal PG4a attached and contribute to paying the statistician.

3. The ‘MANUFACTURER’-acknowledges that THE RESEARCH INSTITUTION’ will have no financial obligations or commitments to the ‘MANUFACTURER’ what so ever as a result of conducting this study.

4. The ’MANUFACTURER’-(with the exception of Section 1.2) may not award or incentivize the study or its related parties in any manner what so ever, nor remunerate, award or offer any financial or other donation or gift to any of those involved with the study.

5. The ’MANUFACTURER’-will finance the statistical analysis of the study results to a maximum of R 3’200.00.

Section 2 – Academic processes and outcome

2.1 The FRC has approved the above mentioned Research Supervisor who in conjunction with the Research Student are the sole contributors to the academic content, procedures, results and findings of the study based on the prescribed data analysis in the research proposal, barring amendments required by the approved research examiners appointed by the RESEARCH INSTITUTION.

2.2 The ‘MANUFACTURER’ acknowledges that the findings upon completion of the study (as determined by the Research Student and Research Supervisors and according to the protocol stated in the attached research proposal) will be final and non-negotiable.

The ‘MANUFACTURER’-acknowledges further that it has no authority over the outcome of this study and may not influence the findings or the reporting thereof in any matter.

2.3 Any modification or deviation from the approved research proposal must be applied for in writing, endorsed by both the Research Student & Supervisors and Head of Department before serving before the FRC/IREC, the final say therein will be determined by the FRC/IREC.

2.4 The ‘MANUFACTURER’-acknowledges that it may not influence or make any change to the approved research protocol/proposal.

Section 3 – Publication of findings

3.1 The findings and outcome of the above mentioned study remain the intellectual property of the ‘RESEARCH INSTITITION’ indefinitely. The study will be published in the format of a hard bound dissertation which will be placed in the DUT library.

3.2 Publication of the findings of this study in a journal or other scholarly medium will be a the discretion of the Research student and /or Research Supervisors who will determine the appropriate medium and place of publication as well as content of the publication. Authorship of any scholarly output originating from this study of the Research Student and Research Supervisors and other collaborators appointed by the Research Student and/or the Research Supervisors. Such scholarly publication must include the names of the Researcher and the Research Supervisor as well as the ‘RESEACH INSTITUTION’. The ‘MANUFACTURER’ has the right to request publication of the research results by the student or its supervisor in a refereed journal within one year after completion of the study.

3.3 Any reference what so ever to the findings of this study if quoted or mentioned in any format must make formal reference to the respective dissertation its official title and its author(s) and the owners of the intellectual property thereof i.e. the ‘RESEARCH INSTITITION’.

3.4 Any reference what so ever to any secondary publication arising from this original study must make formal reference to the respective dissertation its official

title and its author(s) and the owners of the intellectual property thereof i.e. the ‘RESEARCH INSTITUTION’

3.5 The ‘MANUFACTURER’-may make reference to the outcome of this study in the prescribed manner mentioned in section 3.3 and 3.4 undertaking 3.1 and 3.2.

Section 4 – Indemnity

4.1 The Research Student, the Research Supervisor and the research facilities and its staff are duly covered by the ‘RESEARCH INSTITUTION’ insurance policy pertaining to public liability, injury or harm which may occur as a result of conducting this study.

4.2 The ’MANUFACTURER’-undertakes to indemnify the ‘RESEARCH INSTITUTION’ with regard to any outcome, incidents, injury or harm which occurs as a result of the conduction of this study including the results of the study and publication thereof. This indemnification is only valid if the product is used according to the description on the label.

Section 5

5.1 Ethical clearance of the proposed study will be granted by the DUT IREC (such ethical clearance become invalid should there be any deviation from the approved research methodology described in the research proposal attached).

5.2 The ‘MANUFACTURER’ undertakes to abide by the DUT Research Committee Research Ethics Policy and Guidelines (APPENDIX B).

5.3 In addition to 5.2 the ‘MANUFACTURER should note and refer to **Section 1.4,2 & 3** of this document.

I, David Gerber (V-Tech, Chief Technical Officer) ,hereby in my official capacity of Health Tech Laboratories hereby agree to abide by the regulations stated in this memorandum of understanding between the MANUFACTURER and the RESEARCH INSTITUTION

David Gerber (V-Tech, Chief Technical Officer 6 August 2013

Signature of the official representative of the MANUFACTURER Date

I, Miss Cleo Prince hereby in my capacity as the research study herby agree to abide by the regulations in this memorandum of understanding between the MANUFACTURER and the RESEARCH INSTITUTION

Signature of Research Student