CORRELATION OF INTESTINAL HYPERPERMEABILITY AND SEBORRHEIC DERMATITIS

PHAISIT TRAKULKONGSMUT

MASTER OF SCIENCE

PROGRAM IN ANTI-AGING AND REGENERATIVE MEDICINE

MAE FAH LUANG UNIVERSITY

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2011

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Thesis Title	Correlation of Intestinal Hyperpermeability and Seborrheic Dermatitis
Author	Phaisit Trakulkongsmut
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ABSTRACT

Background: Seborrheic dermatitis (SD) is considered one of the most frequent chronic inflammatory skin disorders. The etiology of seborrheic dermatitis is not fully understood but is known to involve various factors such as genetics, stress, drugs, neurological disorder, nutritional disorder, weather and immunity defect. An increased intestinal permeability or leaky gut has been proposed as possible culprits of seborrheic dermatitis but the evidence remain elusive. Many works on increased intestinal permeability in patients with atopic eczema are available. On the contrary, no data on increased intestinal permeability in patients with seborrheic dermatitis can be found. The lack of defined data on the intestinal permeability in patients with seborrheic dermatitis encourage to perform the present study.

Objective: To study the correlation between seborrheic dermatitis and intestinal permeability

Method: The study design was a cross-sectional study. Sixteen healthy volunteers and sixteen patients with a diagnosis of seborrheic dermatitis were recruited from the outpatient department (OPD), Mae Fah Luang University Hospital and by local advertisement. The diagnosis of seborhheic dermatitis is based on clinical features by dermatologist. 16 seborrheic dermatitis patients with mild to moderate severity evaluated by Seborrhea Areas Severity Index

(SASI score). Absorption of lactulose and mannitol was measured in 16 patients with seborrheic dermatitis and healthy control subjects by using intestinal permeability test.

Result: There was no significant difference between mean mannitol excretion in patients with seborrheic dermatitis (mean 22.75 ± 2.14) and the healthy control subjects (mean 22.39 ± 2.02) ($p = 0.621$). The mean lactulose excretion in the patients with seborrheic dermatitis (mean 0.46 ± 0.09) was significantly higher than that of the healthy control subjects (mean 0.29 ± 0.06) ($p < 0.001$). Lactulose/mannitol excretion ratios (L/M Ratio) in the patients with seborrheic dermatitis, range 0.015-0.031 (mean 0.021 ± 0.005) were significantly higher than those of the healthy control subjects, range 0.010-0.022 (mean 0.013 ± 0.003) ($p < 0.001$). One patients with seborrheic dermatitis had L/M ratio outside the normal range.

Conclusion: These data indicate that small intestinal permeability is increased in patients with seborrheic dermatitis. Impairment of the intestinal mucosal barrier appear to be involved in the pathogenesis of seborrheic dermatitis. There was no correlation between either seborrheic dermatitis's severity or the excretion ratio.

Keywords: Seborrheic dermatitis / Intestinal permeability / Lactulose / Mannitol

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CHAPTER 1

INTRODUCTION

1.1 Background and Rationale

The Gastrointestinal mucosal me0mbrane surface is the largest interface between the internal structures of our bodies and the external world. It covers more than 320 square meters, which is over 150-fold greater than the surface area of the skin (Bengmark, 1998; Takahashi & Kiyono, 1999). Over a life time, the average person ingests more than 25 tons of food that provide the nutrients each of us need to survive; however, this food may also contain bacteria, viruses, and toxins. The small intestine which is one of the gastrointestinal tract is important organ in term of long-term health of the human body. Because it is the ultimate area for the digestion and assimilation of food thus it is contact with food and antigens from the outside world, yet also intimately contact with the bloodstream. The absorptive and protective mechanisms are highly developed to facilitate the absorb nutrients, while blocking entrance of potentially harmful antigens to the bloodstream via the intestinal epithelial barrier and immune mechanisms.

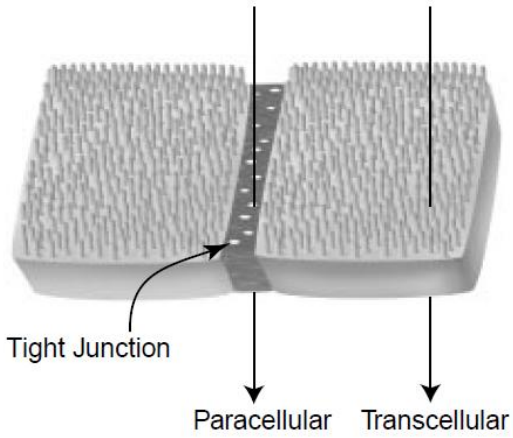
Normally, The intestinal epithelial barrier has 3 major functions; (1) Absorption-transporting fluids, electrolytes, nutrients selectively across the intestinal wall; (2) Protection-separating larger, potentially toxic, antigenic, pathogenic molecules or organisms from passing into the bloodstream; (3) Immune function is supplied by complex mechanisms which support one another : gut-associated lymphoid tissue (GALT), intraepithelial lymphocytes (IELs) and intestinal secretion (mucus, lysozymes, defensins, antimicrobial peptides, and secretory IgA). Throughout the entire length of the small intestine are patches of lymphoid tissue called Peyer's patches, collectively called GALT which accounts for greater than 60% of all immune activity in the body (Brandtzaeg, 1998; Takahashi & Kiyono, 1999). Secretory IgA also plays an important

role binding to bacteria and other antigens, preventing their attachment to epithelial cells, and facilitating their disposal. A decrease in secretory IgA causes increased bacterial adherence, increased intestinal permeability, and bacterial translocation across the intestinal wall. Disruption of any of these factors can cause an increase in intestinal permeability.

Nutrients are absorbed from the lumen via 2 pathways: through the intestinal epithelial cells or enterocytes (transcellular, controlled by the cell membrane) and via the junctions between cells (paracellular, controlled by the permeability tight junctions) (Figure 1.1). Over 85% of the passive transport of molecules is paracellular (Crissinger, Kvietys & Granger, 1990; Madara, 1990). The intestinal lining is supposed to have tight junctions between the intestinal epithelial cells (Nusrat, Turner & Madara, 2000) The tight junctions located at the base of epithelial microvilli are the physical regulator of passive absorption of molecules. In a normal healthy intestine, the tight junctions constitute a barrier that provides limited access for substances from the outside (lumen) to be absorbed inside the body. The intestinal epithelial cells must establish them to seal off the barrier from passage of large molecules. The number and density of tight junctions regulate the diffusion of molecules. When they become destroyed by ulceration or inflammatory process between cells, thus increasing paracellular transport. This allow toxins, antigens, large molecules, and microorganisms to leak from the intestine into bloodstream. This condition is known as intestinal hyperpermeability or leaky gut (DeMeo, Mutlu, Keshavarzian & Tobin, 2002; Gardner, 1998; Thomson, Jarocka-Cyrta & Faria, 1997).

Intestinal hyperpermeability or leaky gut describes a pathological increase in permeability of the intestinal mucosa, subsequent to the loss of intestinal mucosa integrity. It is caused by exposure to substances which damage the tight junctions between intestinal epithelial cells and increases passive, paracellular absorption. The common causes of damage are non-steroidal anti-inflammatory drugs (NSAIDs), ethanol, cytotoxic drugs, antibiotics, viral and bacterial gastroenteritis. This can be a direct effect (NSAIDs, ethanol, cytotoxic drugs) or and indirect effect as with bacterial overgrowth associated with antibiotic therapy (Cappell & Simon, 1993). Leaky gut or intestinal hyperpermeability causes increased absorption of toxin, antigens, inflammatory mediators, large molecules and pathogenic microorganisms. Theses agents can cause local and systemic reactions associated with a broad range of chronic diseases. In some cases, atrophic changes in the mucosal epithelium can lead to the seemingly paradoxical condition

of malabsoption of essential nutrients concurrent with increased permeability of pathogenic substances.



From Miller, A. L. (1997). The pathogenesis, clinical implications, and treatment of intestinal hyperpermeability. **Alternative Medicine Review, 2**(5), 330-345

Figure 1.1 Intestinal absorption pathway.

Intestinal permeability (IP) is the mucosal capacity to allow the passage of molecules from the intestinal lumen to the blood stream. The lactulose-mannitol permeability test is one of the methods most widely used to diagnose intestinal permeability defects because it is simple and reliable to assess many clinical conditions (Dastych, Novotna & Cihalova, 2008; Farhadi, Keshavarzian & Fields, 2006). The permeation of water-soluble molecules through the intestinal mucosa can occur either through cells (transcellular upatake), or between cells (paracellular uptake). The rate limiting barrier is the tight junction between cells. Thus, tight junctions help maintain epithelial integrity. Recent studies have examined the sensitivity and specificity of the lactulose-mannitol (L/M) test for the diagnosis of intestinal permeability defects in a number of specific conditions. A 2008 controlled clinical trial found that the L/M ratio showed 100% specificity and 89.5% sensitivity in assessing intestinal permeability defects in patients with Crohn's disease (Dastych et al., 2008). Lactulose-mannitol intestinal permeability test is being utilized in assessment of gut permeability in a wide range of conditions, including eczema, food

sensitivity, pancreatitis, Crohn's disease and cirrhosis. Lactulose-mannitol intestinal permeability is assessed non-invasively by measuring the urinary excretion of orally administered test substances, chosen because they are non-toxic, not degraded, not metabolized or not normally present in urine but completely excreted and easy to measure.

Recent studies suggest that the increased IP is significantly increased in a number of health conditions or disease processes, including eczema (Caffarelli, Cavagni, Menzies, Bertolini, & Atherton, 1993; Pike, Heddle, Boulton, Turner & Atherton, 1986; Przybilla & Ring, 1990; Rosenfeldt, Benfeldt & Valerius, 2004), urticaria (Paganelli, Fagiolo, Cancian & Scala, 1991), psoriasis (Hamilton et al., 1985), asthma (Benard, Desreumeaux & Huglo, 1996), rheumatoid arthritis (Fagiolo, Paganelli & Ossi, 1989; Mielants, De Vos & Goemaere, 1991; Smith, Gibson & Brooks, 1985), ankylosing spondylitis (Smith et al., 1985), acute gastroenteritis (Ioslauri, Juntunen & Wiren, 1989), post-surgery (Riddington, Venkatesh & Boivin, 1996), alcoholism (Bode, C. & Bode, J. C, 2003; Purohit, Bode, J. C. & Bode, C., 2008), food allergy (Heyman, 2005; Husby, Jensenius & Svehag, 1986; Pena & Crusius, 1998; Ventura, Polimeno & Amoruso, 2006), pancreatic dysfunction (Mack, Flick & Durie, 1992), celiac disease (Festen, Szperl & Weersma, 2009; Visser, Rozing & Sapone, 2009), inflammatory bowel disease (Mankertz & Schulzke, 2007; McGuckin, Eri & Simms, 2009; O'Mahony, Anderson, Nuki & Ferguson, 1992), iritable bowel disease (Zeng, Li & Zhen, 2008), fibromyalgia (Goebel1, Buhner, Schedel1, Lochs & Sprotte, 2008), chronic fatigue syndrome (Maes, Mihaylova & Leunis, 2007), migraine (Scarpellini, 2009) and depression (Maes, Kubera & Leunis, 2008). Increased IP may be implicated in the pathogenesis of several diseases and appears to correlate with a number of diseases.

Seborrheic dermatitis (SD) is considered one of the most frequent skin disorders and it is one of the most conditions for which patients consult a dermatologist. Seborrheic dermatitis is considered as one of the endogenous eczema. Seborrheic dermatitis is a chronic, relapsing inflammatory cutaneous disease characterized by erythema covered with yellow gray scales in the affected areas. The lesions are mainly located in areas containing a large number of sebaceous glands such as the mid-facial region, scalp, and certain areas of the trunk. It typically presents on the scalp, lateral sides of the nose, nasolabial folds, eyebrows, glabella, ears, upper chest and back (Plewing, & Janssen, 2008). Dandruff is considered to be the mildest or perhaps initial form of

seborrheic dermatitis (Gupta, Ryder, Nicol & Cooper, 2003). The course of seborrheic dermatitis involves periods of remission and exacerbation. However, the disease rarely causes serious complications, it always leads to a marked aesthetic deterioration that lead to emotional and social difficulties. Seborrheic dermatitis can have an effect on the quality of life of affected individuals. There is greater impairment of quality of life in patients with more severe symptoms, with a greater effect observed in women (Peyri & Lleonart, 2007).

The absence of standardized diagnostic criteria, coupled with such extreme variability of disease expressiveness, are likely to introduce significant variability of estimates of prevalence. Estimates of prevalence are limited by the lack of validated criteria for diagnosis or grading of severity (Luigi & Alfredo, 2009). The diagnosis is emphasized on the patient's history and clinical examination. The latest prevalence of seborrheic dermatitis was reported in U.S. population in 2004. The reported prevalence of seborrheic dermatitis in adults with normal immune system is about 1-3%. Applying prevalence rates of 1,000 to 3,000 cases per 100,000 individuals (with normal immune system) to the 2004 U.S. population yields an estimate of between 2.9 million and 8.8 million individuals with seborrheic dermatitis (The Society for Investigative Dermatology & the American Academy of Dermatology Association, 2004). It can appear at any age, the highest prevalence is observed in individuals aged 30-60 years. No epidemiological studies of the disease have been undertaken in Thai and information was unavailable.

This study focuses on seborrheic dermatitis because it is considered one of the most skin disorders and has an impairment of quality of life. The etiology of seborrheic dermatitis is not fully understood but is known to involve various factors. Factors that may increase susceptibility to the disease are genetics, stress, depression, fatigue, weather, and oily skin and hair. Despites its name, seborrheic dermatitis is not associated with excessive secretion of sebum, nor are the sebaceous glands involved. An increased intestinal permeability or leaky gut has been proposed as possible culprits of seborrheic dermatitis but the evidence remain elusive. Many works on increased intestinal permeability in patients with atopic eczema are available. On the contrary, no data on increased intestinal permeability in patients with seborrheic dermatitis can be found. The lack of defined data on the intestinal permeability in patients with seborrheic dermatitis encourage

to perform the present study. The aim of this study is to measure intestinal permeability in patients with seborrheic dermatitis of varying severity.

1.2 Research Objective and Hypothesis

1.2.1 Research Question

Dose the seborrheic dermatitis correlate with increased intestinal permeability ?

1.2.2 Objective

To study the correlation between seborrheic dermatitis and intestinal permeability.

1.2.3 Hypothesis

Seborrehic dermatitis correlates with increased intestinal permeability

1.3 Expected Benefits and Applications

The conclusion from this study will support that seborrheic dermatitis develop associated with increased intestinal permeability. If the seborrheic dermatitis correlates with increased intestinal permeability, we could apply this knowledge to prevent disease or lessen severity of symptoms by approaching to small intestinal health

1.4 Conceptual Framework

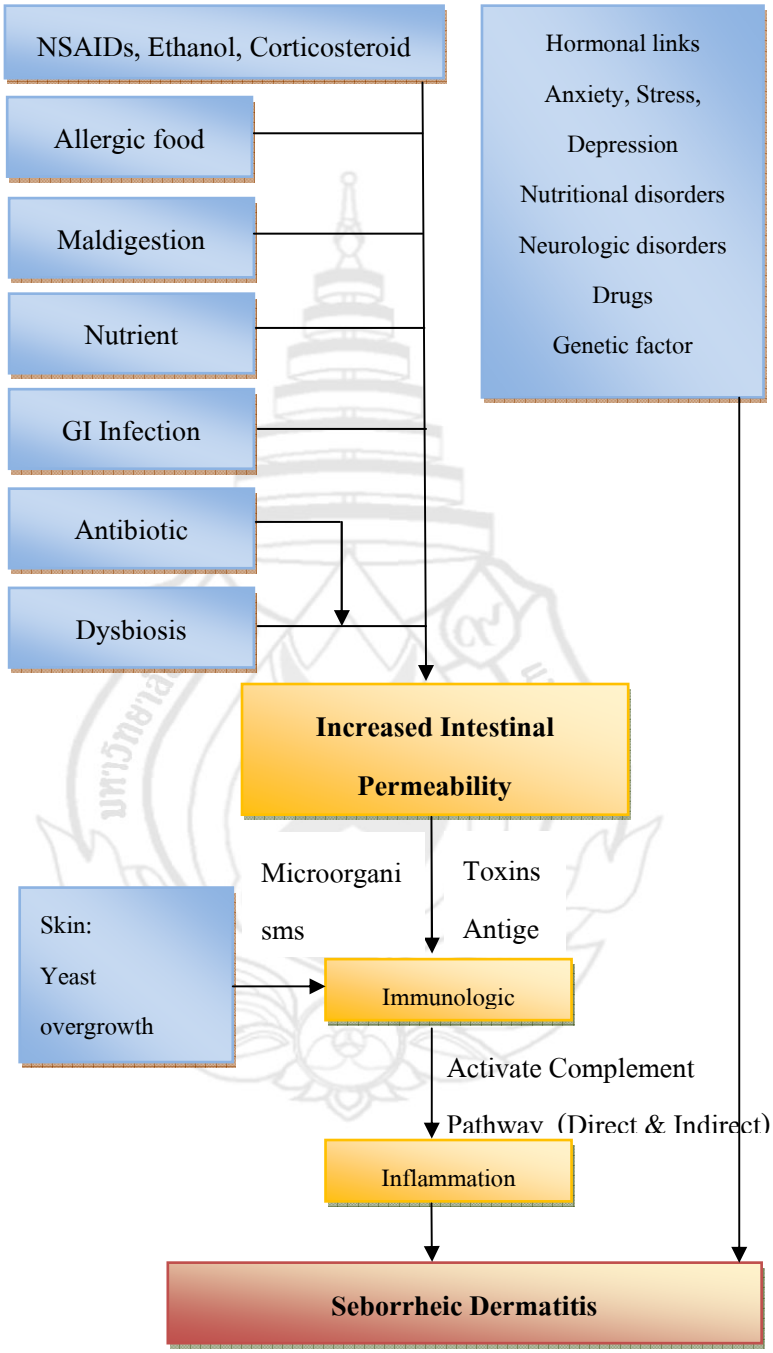


Figure 1.2 Conceptual Framework

1.5 Scope of Research.

1.5.1 Population: Thai population

1.5.2 Sample: Healthy control subjects and patients with a diagnosis of seborrheic dermatitis who attended the outpatient clinic, Mae Fah Luang University Hospital are invited to participate.

1.6 Operational Definitions.

1.6.1 Intestinal permeability: the mucosal capacity to allow the passage of molecules from the intestinal lumen to the blood stream.

1.6.2 Intestinal hyperpermeability or leaky gut: a pathological increase in permeability of the intestinal mucosa, subsequent to the loss of intestinal mucosa integrity. It is caused by exposure to substances which damage the tight junctions between intestinal epithelial cells and increases passive, paracellular absorption.

1.6.3 Tight junction: Mammalian epithelial cells form a series of intercellular junctions along their lateral margins closest to the luminal surface lies the tight junction in order to regulate traffic through this paracellular pathway. These structures are enormously complex in both their lipid and protein constituents. An ever expanding family of proteins are found in the vicinity of these junctions, forming fibrils that cross the plasma membrane to interact with proteins from the adjoining cell. The tight junction serves as a regulated, semipermeable barrier that limits the passive diffusion of solutes across the paracellular pathway between adjacent cells. In some organs, notably the gut and lung, this barrier function is also important to prevent systemic contamination by microbes and toxins that are present in the external environment.

1.6.4 Lactulose-mannitol test: One of the methods most widely used to diagnose intestinal permeability.

1.6.5 Seborrheic dermatitis is considered as one of the endogenous eczema. It is a chronic, relapsing inflammatory cutaneous disease characterized by erythema covered with greasy-looking scales in the affected areas. The lesions are mainly located in areas containing a large number of sebaceous glands such as the mid-facial region, scalp, and certain areas of the trunk. Dandruff is considered to be the mildest or perhaps initial form of seborrheic dermatitis.

CHAPTER 2

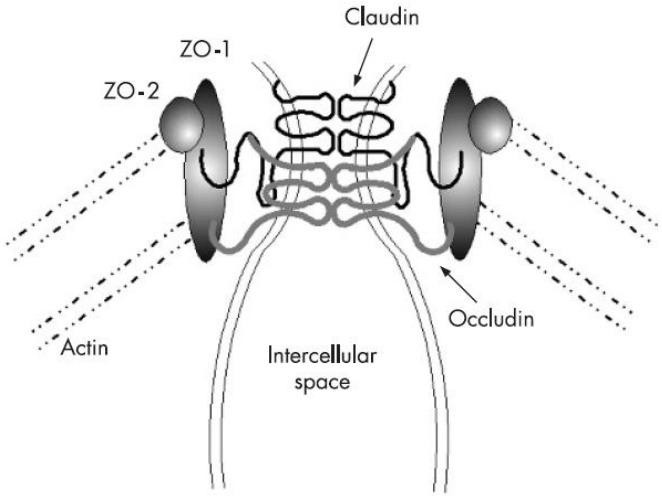
LITERATURE REVIEW

2.1 The Tight Junction as The Intestinal Defensive Barrier

The intestinal epithelial cells form tight junctions between each other (Nusrat et al., 2000). These tight junctions establish a defensive barrier between the molecules within the lumen of the intestinal tract and the bloodstream. The mammalian epithelial cells form the tight junctions along their lateral margins closest to the luminal surface so as to regulate paracellular pathway. These structures are complex in both their lipid and protein components. The proteins are found in these junctions, forming fibrils (claudin and occludin) that cross the plasma membrane to interact with proteins from the adjacent cell. The intracellular side of the epithelial membrane, the carboxyl group of terminal end of these proteins (claudin and occludin) interacts with the other tight junction proteins called ZO1, and ZO2 (see Figure 2.1) (Arrieta, Bistritz, Meddings, 2006). The tight junction serves as a semipermeable barrier that limits the passive diffusion of molecules across the paracellular pathway between adjacent cells. (Anderson & Van Itallie, 1995; Stevenson, 1999). In some organs, the gut and lung, the tight junction or a semipermeable barrier is also important to prevent systemic contamination by microorganisms and toxins that are existent in the external environment. (Mitchell, 2003)

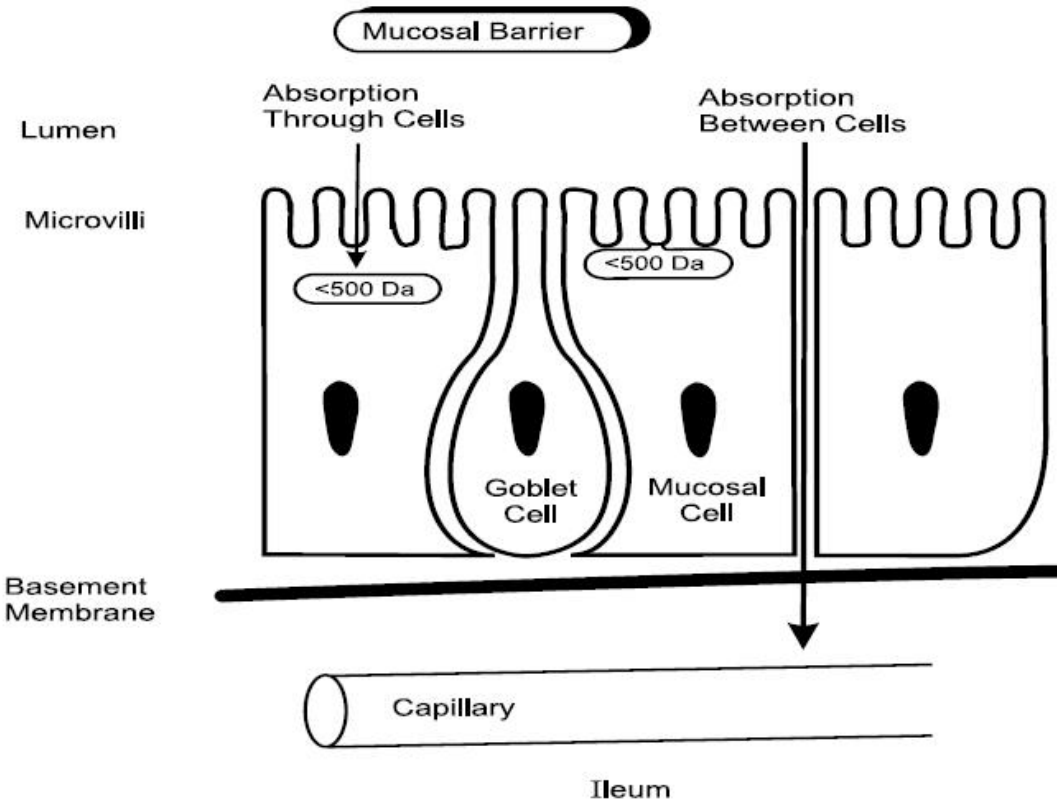
Under normal healthy conditions, nutrients and other small molecules are absorbed through the intestinal mucosal cells by facilitated, active, or passive transport. These small molecules, lesser than 500 Da in size, transport through cells (see Figure 2.2) (Liska, & Lukaczer, 2002). The tight junctions between the enterocytes form the intestinal defensive barrier. When this barrier is destroyed, some larger molecules which are approximately greater than 500 Da in size may leak through these channels. Therefore the larger molecules enter the blood circulation

without passing through the enterocytes, a condition called " increased intestinal permeability or leaky gut". (DeMeo et al, 2002; Gardner, 1998; Thomson et al., 1997).



From Arrieta, M. C., Bistritz, L. & Meddings, J. B. (2006). Alteration in intestinal permeability. **Gut, 55**(10), 1512–1520.

Figure 2.1 Structure of tight junctions



From Liska, D. J. & Lukaczer, D. (2002). Gut restoration and chronic disease. **Journal of American Nutraceutical Association, 5**(4), 20-33.

Figure 2.2 The concept of intestinal permeability in the small intestine

2.2 Factors Associated with Development of Intestinal Hyperpermeability

It is crucial to consider what factors alter permeability of the tight junctions. From now on, it is now recognized that the function of the tight junctions, once considered a static state, is in dynamic state. These epithelial tight junctions open and close all the time in response to a variety of stimuli (Arrieta et al., 2006). A number of drugs, including NSAIDs, antibiotics, chemotherapeutic agents, estrogen, cocaine, and amphetamines can cause intestinal inflammation and increased permeability. This can be a direct effect (NSAIDs, chemotherapy, cocaine, methotrexate), or an indirect effect, as with colitis or bacterial overgrowth associated with antibiotic therapy. Table 2.1

lists some major factors that have been shown to increase intestinal permeability. A number of causative factors of intestinal permeability defects have been identified in the literature

Table 2.1 Factors Associated with Development of Increased Intestinal Permeability

Factors associated with development of increased intestinal permeability
Nonsteroidal anti-inflammatory drugs (NSAIDs) (Jenkins, Trew & Crump, 1991).
Ethanol consumption (Bjarnasorn, Wise, & Peters, 1984; Bode, C. & Bode, J. C, 2003).
Corticosteroid use (Berg, Wommack, & Deitch, 1998).
Antibiotics use (Berg, 1992; Saadia & Lipman, 1996).
Antacid use (Lord & Bralley, 2008).
Cytotoxic drugs. (Pledger, Pearson, Craft, Laker & Eastham, 1988).
Cow's milk intolerance (Troncone, Caputo, Florio & Finelli, 1994).
Intestinal inflammation (Geboes, 1994).
Intestinal infection (Ioslauri et al., 1989).
Ingestion of allergic foods (Dupont & Heyman, 2000).
Maldigestion (Pancreatic insufficiency) (Mack et al., 1992).
Mucosal oxidative stress (Banan, Choudhary & Zhang, 2000).
Nutrient insufficiency (Minzel, n.d.)
Radiation (Coltart, Howard, Wraight & Bleehen, 1988).
Stress (Lampert, 2009).
Smoking (Prytz, Bennoni & Tageson, 1989).
Small intestine bacterial overgrowth (SIBO) or Dysbiosis (Ziegler & Cole, 2007).

2.3 Diseases Associated Intestinal Hyperpermeability

Recent studies suggest that the increased intestinal permeability is significantly increased in a number of health conditions or disease processes, including eczema, urticaria, psoriasis, asthma, rheumatoid arthritis, ankylosing spondylitis, other spondyloarthropathies, food allergy,

asthma, acute gastroenteritis, trauma, post-surgery, alcoholism, pancreatic dysfunction, celiac disease, inflammatory bowel disease, irritable bowel disease, HIV disease, burn injury, endotoxemia, cystic fibrosis, fibromyalgia, chronic fatigue syndrome and migraine. Increased IP may be implicated in the pathogenesis of several diseases and appears to correlate with a number of diseases (Table 2.2)

Table 2.2 Diseases Associated with Increased Intestinal Permeability

Diseases associated with increased intestinal permeability
Inflammatory bowel disease. (Mankertz & Schulzke, 2007; McGuckin et al., 2009; O'Mahony et al., 1992).
Celiac disease (Festen et al., 2009; Visser et al., 2009).
Autism (Lord & Bralley 2008).
Childhood hyperacitivity (Lord & Bralley 2008).
Irritable bowel syndrome (Zeng et al., 2008).
Ankylosing spondylitis (Smith et al., 1985).
Rheumatoid arthritis (Fagiolo et al., 1989; Mielants et al., 1991; Smith et al., 1985).
Eczema (Caffarelli et al., 1993; Pike et al., 1986; Przybilla et al., 1990; Rosenfeldt et al., 2004; Ukabam, Mann & Cooper, 1984).
Urticaria (Paganelli et al., 1991).
Psoriasis (Hamilton et al., 1985).
Food allergy (Heyman, 2005; Husby et al., 1986, Pena & Crusius, 1998; Ventura et al., 2006).
Migraine (Scarpellini, 2009).
Depression (Maes et al., 2008).
Schizophrenia (Wei & Hemmings, 2005).
Asthma (Benard et al., 1996).
Fibromyalgia (Goebel1 et al., 2008).
Chronic fatigue syndrome (Maes et al., 2007).

Atopic Dermatitis (Eczema) has been reported associated increased intestinal permeability. Baseline intestinal permeability measurements of children with eczema are higher than normal individuals and may improve with elimination diet therapy. (Caffarelli et al., 1993; Pike et al., 1986; Przybilla & Ring, 1990; Rosenfeldt et al., 2004; Ukabam et al., 1984). In a study of 15 children with eczema, nine had at least a 75% improvement in their clinical score after a 14-day elimination diet. In the group which showed clinical improvement, the mean permeability was significantly lower than in non-responders ($p < 0.01$). (Caffarelli et al., 1993)

2.4 Seborrheic Dermatitis

The 1971–1974 National Health and Nutrition Examination Survey, which involved a representative sample of persons 1 to 74 years of age in the U.S. population, showed that the prevalence of seborrheic dermatitis, as assessed by a dermatologist, was 11.6% overall. In this sample, the prevalence of clinically significant seborrheic dermatitis was lowest among persons younger than 12 years of age (<1%) and was highest among persons 35 to 44 years of age (4.1%). (Luigi & Alfredo, 2009). Therefore among adults, the peak prevalence is in the third and fourth decades of life. The latest prevalence of seborrheic dermatitis was reported in U.S. population in 2004. Applying prevalence rates of 1,000 to 3,000 cases per 100,000 individuals (with normal immune system) to the 2004 U.S. population yields an estimate of between 2.9 million and 8.8 million individuals with seborrheic dermatitis. (The Society for Investigative Dermatology & the American Academy of Dermatology Association, 2004). No epidemiological studies of the disease have been undertaken in Thai and information was unavailable.

Seborrehic dermatitis is characterized by erythematous patches and greasy scaling, typically presenting on the scalp, the nose, the nasolabial folds, medial aspect of the eyebrows, the glabella, the concha of auricles, the retroauricular areas and chest. Itching is moderate and usually limited to the scalp and the external auditory meatus. Despite its name, sebum excretion in patients with seborrheic dermatitis is not significantly increased when compared with control. The course of the disease waxes and wanes. The disorder may lead to psychological distress, low self esteem, embarrassment and secondary bacterial or fungal infections.

Owing to the absence of standardized diagnostic criteria, the diagnosis is based on the appearance and location of the skin lesions. The diagnosis of seborrheic dermatitis is based on the history and clinical examination.

Despite the high prevalence of seborrehic dermatitis, the etiology remains unknown. However many factors (e.g. hormonal level, fungal infections, nutritional deficits, neurogenic factors) have been implicated with the condition. Recent articles on seborrheic dermatitis have continued to stress that the etiology remains unknown. Although various factors (both exogenous and endogenous) have been described as possible triggers of the disease.

The hormonal link may explain why the condition appears infancy, disappears spontaneously, then reappears more prominently after puberty. (Schwart, Janusz & Janniger, 2006).

The link seems to exist between seborrheic dermatitis and fungi of the genus Malassezia (formerly known as Pitirosporum ovale), which are lipid-dependent, residents of the skin. Yeasts of this genus have been considered potentially pathogenic, since they are present on affected skin, and antifungal agents are useful in treatment. (Deangelis et al., 2005; Heng, Henderson, Barker & Haberfelde, 1990). However, the absence of a correlation between the number of malassezia organisms and the presence of clinical manifestations. (Deangelis et al., 2005) Overgrowth of *M. furfur* may lead to inflammation, either through introduction of yeast derived metabolic products into the epidermis or as a result of the presence of yeast cells on the skin surface. The mechanism of production of inflammation would likely then be through Langerhans cell and T lymphocyte activation by *M. furfur* or its by products. When *M. furfur* comes into contact with serum, it can activate compliment via the direct and alternative pathways and this may play some part in the introduction of inflammation. In seborrheic dermatitis, both normal and high levels of serum antibodies against *M. furfur* have been demonstrated.

Seborrheic dermatitis may be associated with nutritional disorder. An abnormal metabolism of essential fatty acid (transient impaired function of delta 6 desaturase) have been proposed (Tollesson, Frithz, Berg, & Karlman, 1993). Zinc deficiency in paitents with acrodermatitis enteropathica may be accompanied by dermatitis mimicking seborrheic dermatitis of the face. Biotin deficiency, whether secondary to biotinidase or holocarboxylase deficiency has been proposed as possible mechanism.

There is outbreaks of seborrheic dermatitis in periods of anxiety, stress, and depression. (Picardi & Abeni, 2001).

It has been suggested that skin temperature may be responsible for the distribution of seborrheic dermatitis. Seasonal variation in temperature and humidity are related to the course of the disease. An exposure to air conditioning in the work place also had a greater effect on patients of a working age. Although exposure to sunlight is thought to be beneficial in seborrheic dermatitis. (Peyri & Lleonart, 2007).

Seborrheic dermatitis is often associated with a variety of neurological abnormalities. Pointing to a possible influence of the nervous system (neurotransmitter abnormalities). A neurogenic theory for the development of seborrheic dermatitis may account for its association with parkinsonism and other neurologic disorders, including post cerebrovascular accidents, epilepsy, central nervous system trauma, and facial nerve palsy. (Schwart et al., 2006).

Several drugs have been reported to produce seborrheic dermatitis-like lesions, including mehyl-dopa, cimetidine, neuroleptics.

Genetic defect in a zinc finger protein has been considered that associated with seborrheic dermatitis.

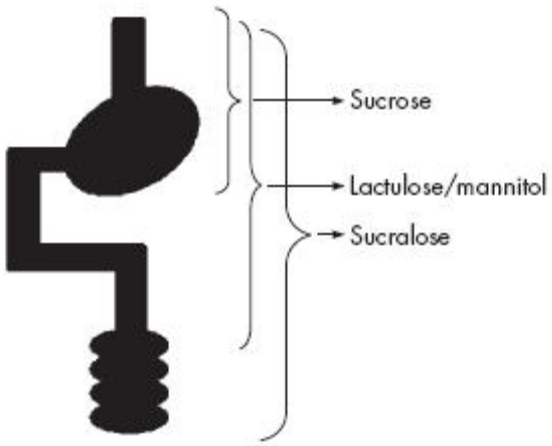
2.5 Measurement of Intestinal Permeability

In the past, there has been an attempt to develop simple non-invasive procedures to evaluate the intestinal permeability of the paracellular pathway. Transportation across this pathway occurs by a non-carrier mediated process and as such depends on several features such as the concentration gradient across the barrier, the surface area of the intestinal epithelium, the time available for permeation and the intrinsic permeability properties of the barrier.

A wide variety of probes have been utilized to determine paracellular permeability properties. Typically, the probes are usually small, water soluble, non-charged compounds that are not destroyed in the gut, are non-toxic, not metabolized once absorbed, and must be cleared only by the kidney into the urine. Ultimately, they should be easily detectable in urine and easily separated from dietary compounds. (Bjarnason, Macpherson, Hollander, 1995). For instance, sucrose is a useful probe for determining permeability characteristics of the gastroduodenal

region. Distal to the gastroduodenal region, sucrose is rapidly hydrolyzed by sucrase-isomaltase (Meddings, Sutherland & Byles, 1993). The traditional small intestinal permeability probes, lactulose, mannitol, rhamnose, or cellobiose are degraded by the bacterial flora of the colon. In order to evaluate colonic permeability properties, Cr-EDTA (nondegraded radiolabeled chelates) or sucralose are selected because they are stable in the colon. (Meddings & Gibbons, 1998). (Figure 2.3)

Lactulose is the most widely used disaccharide probe for intestinal permeability measurement and is commercial available at a reasonable price as 67% wt/vol syrup. Cellobiose should be avoided because there is some small intestinal cellobiase activity. Mannitol and L-rhamnose are monosaccharide probe but mannitol is more commonly used than L-rhamnose. Because the urinary excretion of mannitol is almost complete between 67-100%. On the contrary, the urinary excretion of L-rhamnose 24 hours after administration is incomplete 74% approximately. (Bjarnason et al., 1995).



From Arrieta, M. C., Bistritz, L. & Meddings, J. B. (2006). Alteration in intestinal permeability. **Gut, 55**(10), 1512–1520.

Figure 2.3 Probes specific GI tract region of permeability measurement

Several means are available to investigators studying the mechanisms responsible for the development of intestinal hyperpermeability under normal or pathologic conditions.

Recent studies have examined the sensitivity and specificity of the lactulose-mannitol (L/M) test for the diagnosis of intestinal permeability defects in a number of specific conditions. A 2008 controlled clinical trial found that the L/M ratio showed 100% specificity and 89.5% sensitivity in assessing intestinal permeability defects in patients with Crohn's disease and the L/M ratio showed 88.5% specificity, 84.2% sensitivity in liver cirrhosis. (Dastych et al., 2008). Lactulose-mannitol intestinal permeability test is being utilized in assessment of gut permeability in a wide range of conditions, including food sensitivities, pancreatitis, Crohn's disease and cirrhosis.

Measurement of intestinal permeability is based on the urinary assessment and quantification of orally-ingested molecules which have specific absorption characteristics but are not metabolized by the body. The most common clinically-used test of intestinal permeability is the lactulose/mannitol test. Lactulose and mannitol are water soluble molecules which are not metabolized by the body and are excreted intact in the urine. Lactulose (mol. wt. 342), a disaccharide consisting of galactose and fructose, is not well absorbed, and thus should not be present in large amounts in the urine. Mannitol (mol. wt. 182), a monosaccharide, is normally well absorbed and usually is presented in greater amounts in the urine. Mannitol is thought to be passively absorbed via the transcellular route, while lactulose, the larger molecule, is absorbed in small amounts by the paracellular (tight junction) route. (Miller, 1997).

The test is based on an oral challenge with lactulose and mannitol, two non-metabolized sugar molecules, to permeate the intestinal mucosa. Since these sugars are not metabolized, any absorbed sugar is fully excreted in the urine within 6 hours. The intestinal permeability test requires an overnight fast. Nothing, including water should be consumed after 11 p.m. To perform the test, the patient mixes premeasured amount of lactulose and mannitol and drinks the challenge substance. The urine is collected, and concentrations of the two sugars are measured.

Under normal conditions, small molecules like the monosaccharide mannitol are readily absorbed through the intestinal mucosa by passive diffusion and serves as a marker of transcellular uptake. In contrast, larger molecules like the disaccharide lactulose are normally not absorbed by cell membranes but can be slightly absorbed by tight junction apparatus between cells. Lactulose serves as a marker of paracellular uptake or mucosal integrity. (Figure 2.4)

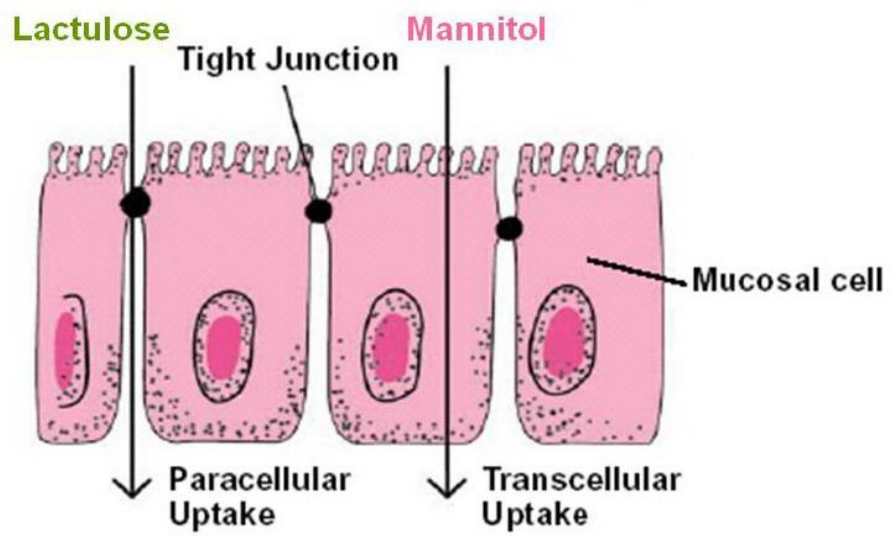


Figure 2.4 Lactulose and mannitol absorption

The amount of lactulose and mannitol recovered in the urine after 6 hours and the ratio between them are used as indicators of IP and mucosal barrier function. In healthy intestine, the mean absorption of mannitol is 14% of the administered dose, whereas the mean absorption of lactulose is less than 1%. Low level of mannitol and lactulose indicate malabsorption. Elevated levels of lactulose and mannitol are indicative of leaky gut syndrome (Lord & Bralley, 2008).

The lactulose/mannitol ratio is a useful parameter. An elevated ratio indicates that the pore size of the intestinal mucosa has increased, allowing access of macromolecules, antigens, toxins, and pathogenic bacteria to the body. The normal lactulose/mannitol ratio recovered in urine is < 0.03. Thus, an elevated ratio means that excessive lactulose was absorbed, indicating leaky gut syndrome (Lord & Bralley, 2008).

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Population and Sample

3.1.1 Population: Thai population (male or female)

3.1.2 Sample: Normal healthy controls and patients with a diagnosis of seborrheic dermatitis who attended the outpatient clinic, Mae Fah Luang University Hospital are invited to participate. The diagnosis of seborhheic dermatitis is based on clinical features by dermatologist. There is still no laboratory test or definite marker for establishing the diagnosis of seborrheic dermatitis. Clinical evaluation is the most important.

3.1.3 Sample size determination (Two sample)

Precision 90% CI (specify α error)

$$n = \frac{Z_{\alpha}^{2} (\sigma_1^{2}+\sigma_2^{2})}{d^2}$$

α = Probability of type I error (1-sided) = 0.1 ; $z_{0.1} = 1.28$

σ = Standard deviation of intestinal permeability

(Intestinal permeability in patients with eczema; $\sigma_1 = 0.13$)

(Intestinal permeability in healthy control; $\sigma_2 = 0.01$)

d = Allowable error in estimating (margin of error) = 0.03

$$n = \frac{(1.28)^2 (0.013^2+0.01^2)}{(0.03)^2} = 31$$

3.1.4 Sample Selection

3.1.4.1 Inclusion criteria:

1. Healthy control subjects aged 20-60 years without any evidence of gastrointestinal or skin diseases.
2. Patients with seborrheic dermatitis aged 20-60 years
3. Any genders.
4. Healthy control subjects and patients were informed consent and sign informed consent of the intestinal permeability studies. Each subject had all possible risks and benefits explained to them in depth.

3.1.4.2 Exclusion criteria:

1. Pregnant and breastfeeding women
2. Subjects taking drugs known to alter intestinal permeability (NSAIDs) ,aspirin, corticosteroid, antacids, H_2 blockers, proton pump inhibitors, chenodeoxycholic acid, cytotoxic drugs) 3 months before the IP test.
3. Subjects ingesting alcohol at least 1 month before the IP test
4. Smokers
5. Subjects who have used antibiotics in other than local applications within the last 3-month period
6. Diabetes mellitus
7. Malignancy
8. GI diseases (e.g. Gastroenteritis, IBD, IBS)

3.2 Equipments

3.2.1 Observation & Measurement

3.2.1.1 Research variables:

1. Independent variable: Seborrheic dermatitis
2. Dependent variable: Intestinal permeability
3. Controlled variables: drugs known to alter intestinal permeability, alcohol, and smoking.

3.2.1.2 Equipments :

1. Record forms : record patient's history and physical examination.
2. Intestinal permeability kit (request form, brown plastic bottle containing 10 ml solution of mannitol 1.5g/lactulose 2.5g, plastic droppler, 10 ml plastic tube)
3. Informed consent
4. Intestinal permeability test instruction document.

3.2.2 Research Methodology

3.2.2.1 Sixteen healthy control subjects and sixteen patients with seborrheic dermatitis aged between 20-60 years are enrolled in the study at Mae Fah Luang University Hospital, Bangkok. The diagnosis of seborrheic dermatitis is based on clinical features by dermatologist.

3.2.2.2 All patients are performed complete physical examination and history taking concerning signs, symptoms, severity, past and current medication, underlying diseases, alcohol drinking and smoking by physician in order that their qualifications are fallen into inclusion criteria.

3.2.2.3 Explaining the procedure of intestinal permeability test to all subjects and give them the intestinal permeability collection instruction document. They all were informed consent to the intestinal permeability study. Female subjects should not collect urine during menstrual period.

3.2.2.4 All subjects are fast overnight (do not eat any food from 11 pm onwards), water may be consumed during this time. After getting up in the morning and passing the morning urine, thereafter the procedures are performed by using two non-metabolized sugar 10 ml solution containing 2.5 g lactulose and 1.5 g mannitol. To perform the test, subjects have to add warm water to the syrup in the brown plastic bottle of premeasured amount of lactulose and mannitol until ¾ full and replace the lid firmly and shake the container vigorously to dissolve the white powder, thereafter drink the challenge substance.

3.2.2.5 Over the collection time of this test (6 hours after ingestion of lactulose and mannitol) avoid food containing fructose as these will affect the test results. Common food

containing fructose include fruit, fruit juice and honey. It is advisable to check food labels for added fructose.

3.2.2.6 For the following 6 hours, all urine must be collected into 4 liter urine collection bag and stored in 4°C in the refrigerator. The total urine volume is read from the scale on the side of the bag and recorded on the request form. Using the plastic dropper, transfer 10 ml of well-mixed urine from the bag into the 10 ml urine specimen tube by nurse or medical technician. Label the tube with patient's names, the date and time. Place the 10-ml samples of urine in the padded envelope and seal it. Being stored in 4°C in refrigerator until the chromatographic analysis

3.2.2.7 Analyzing lactulose percent recovery, mannitol percent recovery, the ratio between lactulose and mannitol (L/M ratio) are used as indicators of intestinal permeability. Analyzing the correlation of intestinal permeability and severity of seborrheic dermatitis by means of statistics.

3.3 Data Collection

Data collection is performed in patients whom was provided signed informed consent prior to inclusion in the study by the researcher.

3.3.1 Details of the collected data

3.3.1.1 Name, gender and age

3.3.1.2 The body areas affected by seborrheic dermatitis in the study population (scalp, eyebrows, glabella, bridge of the nose, nasolabial folds, the concha of auricles, retroauricular area, chest, and other areas)

3.3.1.3 The severity of the seborrheic dermatitis lesions was evaluated using the Seborrhea Area and Severity Index (SASI). The SASI rates both the degree of involvement and severity for seborrheic dermatitis and dandruff on the head as a single number on a scale of 1 to 48. The area is divided into the scalp and facial areas (including ears) that are accorded equal weighting for purposes of the rating formula (as described in Figure 3.1)

3.3.1.4 History of smoking and alcohol drinking

3.3.1.5 Underlying diseases

3.3.1.6 Past and current medication

3.3.1.7 Intestinal permeability results: lactulose percent, mannitol percent, and lactulose and mannitol excretion ratio (L/M ratio)

3.3.2 Laboratory investigations

Lactulose/mannitol intestinal permeability test

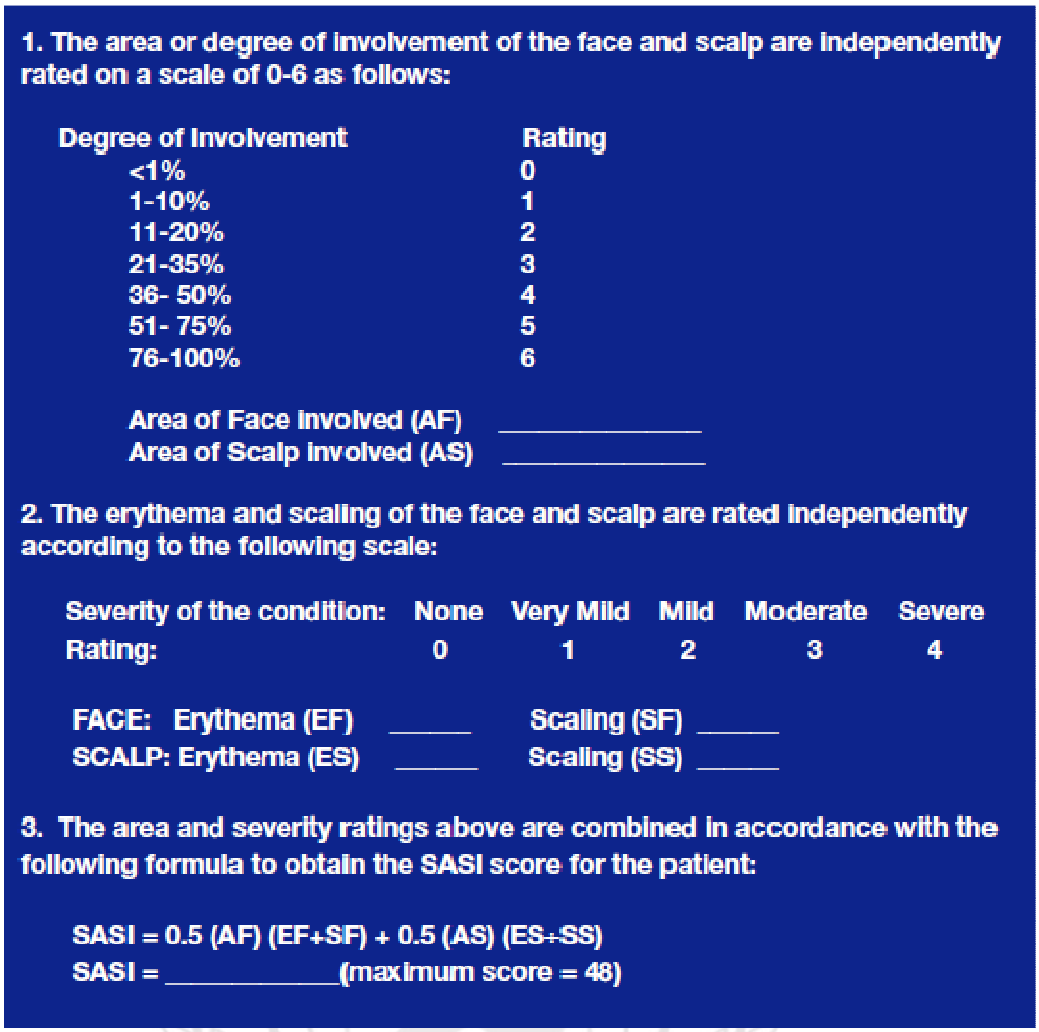
3.3.3 Data Analysis

3.3.3.1 The basic data are presented as percent, mean, and standard deviation.

3.3.3.2 If data is normally distributed, mannitol percent excretion, lactulose percentexcretion and lactuolse/mannitol excretion ratio (L/M ratio) between control subjects and patients are compared using t-test.

3.3.3.3 If the data does not appear to follow a normal distribution, mannitol and lactulose percent excretion between control subjects and patients are compared using Mann-Whitney U test

3.3.3.4 The correlation between the severity of seborrheic dermatitis and the intestinal permeability (Lactulose/mannitol) are evaluated by Pearson test.



1. The area or degree of involvement of the face and scalp are independently rated on a scale of 0-6 as follows:

Degree of Involvement	Rating
<1%	0
1-10%	1
11-20%	2
21-35%	3
36- 50%	4
51- 75%	5
76-100%	6

Area of Face involved (AF) _____
Area of Scalp involved (AS) _____

2. The erythema and scaling of the face and scalp are rated independently according to the following scale:

Severity of the condition:	None	Very Mild	Mild	Moderate	Severe
Rating:	0	1	2	3	4

FACE: Erythema (EF) _____ Scaling (SF) _____
SCALP: Erythema (ES) _____ Scaling (SS) _____

3. The area and severity ratings above are combined in accordance with the following formula to obtain the SASI score for the patient:

SASI = 0.5 (AF) (EF+SF) + 0.5 (AS) (ES+SS)
SASI = _____(maximum score = 48)

From Smith, S. A., Baker, A. E. & Williams, J. H. (2002). Effective treatment of seborrheic dermatitis using low dose, oral homeopathic medication consisting of potassium bromide, sodium bromide, nickel sulfate, and sodium chloride in a double-blind, placebo-controlled study. **Alternative Medicine Review, 7**(1), 59-67.

Figure 3.1 Seborrhea Area and Severity Index (SASI)

CHAPTER 4

RESULTS

The study design was a cross-sectional study. The study was initiated under a hypothesis that there is a correlation between seborrheic dermatitis and increased intestinal permeability (leaky gut) that were obtained from lactulose and mannitol test. The results from the study are categorized into demography, clinical characteristics of patients with seborrheic dermatitis and intestinal permeability testing result.

4.1 Demography

Sixteen healthy volunteers and sixteen patients with a diagnosis of seborrheic dermatitis were recruited from the outpatient department (OPD), Mae Fah Luang University Hospital and by local advertisement. The diagnosis of seborhheic dermatitis is based on clinical features by dermatologist

Table 4.1 Demography

Variables	Seborrheic dermatitis		Healthy control		p-value
	(N=16)	%	(N=16)	%	
Gender					0.077
Male	10.00	62.50	5.00	31.25	
Female	6.00	37.50	11.00	68.75	
Age (years)					
Median(year) ± SD	39±8.82		37.94±9.41		0.744
Max-Min	27-57		27-60		

Table 4.1 (Continued)

Variables	Seborrheic dermatitis		Healthy control		p-value
	(N=16)	%	(N=16)	%	
Underlying disease					1.000†
None	15.00	93.75	0.00	100.00	
Yes	1.00	6.25	0.00	0.00	
Hepatitis B	0.00	6.25	0.00	0.00	
Occupation					0.269†
Account manager	1.00	6.25	0.00	0.00	
Business owner	3.00	18.75	2.00	12.5	
Dentist	1.00	6.25	0.00	0.00	
Doctor	6.00	37.5	3.00	18.75	
Nurse	1.00	6.25	1.00	6.25	
Officer	4.00	25.00	10.00	62.5	

Note. There is no difference significantly in demographic data between patients with seborrehic dermatitis and healthy controls. Demographic data among two groups were compared using Independent T-test, Chi-square test and Fisher exact test.

During a study period, a total of 32 participants were studied included 16 patients with seborrheic dermatitis and 16 healthy control subjects. The mean age of patients with seborrheic dermatitis (±S.D.) was 39 ± 8.82 years (range, 27-57 years). The male : female ratio was 1.67 : 1.00 (10 males: 6 females). The mean age of the healthy control subjects (±S.D.) was 37.9±9.41 years (range, 27-60 years). The male : female ratio was 1 : 2.2 (5 males : 11 females). The patient and healthy control groups were comparable in terms of age and gender. There was no difference in age or sex between the groups.

Out of 16 patients with seborrheic dermatitis, only one patient had Hepatitis B and the remaining 15 patients did not have any other underlying diseases. In seborrheic dermatitis group,

no intestinal diseases or symptoms were noted. All patients met the clinical features of seborrheic dermatitis diagnosed by dermatologist. There was no underlying disease in all of healthy control subjects. None had symptoms of gastrointestinal disease. Most of healthy control subjects were recruited from university officers.

During the study period, None of the subjects discontinued due to possible side effects of lactulose and mannitol. Thirty-two subjects completed the entire study.

4.2 Clinical Characteristics of Patients with Seborrheic Dermatitis

Table 4.2 Clinical Characteristics of Patients with Seborrheic Dermatitis

Variables	Seborrheic dermatitis	
	(N=16)	%
Signs and symptoms		
Erythema	16	100.00
Scaling	12	75.00
Pruritus	5	31.25
Affected area		
Scalp or at the edge of the scalp	16	100.00
Glabella or Eyebrows	8	50.00
Nasolabial folds	6	37.50
Nose	3	18.75
Ears (Concha of the auricles, retroauricular area)	6	37.50
Factors that trigger outbreaks		
Inadequate sleep	16	100.00
Stress	16	100.00
Intense sunlight/heat	5	31.25
Colder climate/Exposure to air conditioning	10	62.50

Table 4.2 (continued)

Variables	Seborrheic dermatitis	
	(N=16)	%
Alcohol consumption	2	12.50
Dairy product consumption	12	75.00
Frequency of outbreaks		
1-2 time/month	3	18.75
3-4 time/month	10	62.5
5-6 time/month	3	18.75

Table 4.2 shows the clinical characteristics of patients with seborreheic dermatitis. The most severe symptoms were erythema (100%) and scaling (75%) followed by pruritus (37.5%) The area affected by seborrheic dermatitis in the study group. The most commonly affected area were the scalp (100.0%), glabella or eyebrows (50.0%) followed by ears (37.5%) and nasolabial folds (37.5%). Very few patients had involvement of the nose (18.75%). The total was greater than 100% since more than one area could be affected in the same patient.

Patients were asked to indicate the factors that had been present prior to the outbreaks. Both of the stress and inadequate sleep were the most common factor (100 % in each) followed by dairy product consumption (75%), colder climate/exposure to air conditioning (62.5%), exposure to the intense sunlight/heat (31.25%). Alcohol consumption was less common reported by 12.5% of patients. It is observed that the most common frequency of outbreaks was 3-4 times a month.

Table 4.3 Assessment of Seborrheic Dermatitis According to the Seborrhea Area Severity Index

Patient	Sex	Age	Seborrhea Area Severity Index (SASI) (Maximum Score = 48)
.M.	M	39	23
W.V.	M	43	36
S.L.	M	51	21
K.C.	M	43	24
W.C.	M	30	33
T.R.	F	29	28
A.K	F	47	13
A.A.	F	30	13
S.T.	M	48	16
T.N.	M	57	16
L.T.	F	37	4.5
P.T.	M	30	4.5
P.J.	M	27	8.5
Pi.T.	M	34	28
J.B.	F	38	30
S.S.	F	41	11

The mean score of seborrhea area severity index (SASI) was 18.8, the maximum score in patients was 36, whereas the minimum score was 4.5.

4.3 Intestinal Permeability Testing Results

During the study period, none of the subjects discontinued due to possible side effects of lactulose and mannitol. Thirty-two subjects completed the entire study. All subjects tolerated the oral sugar (lactulose & mannitol) loads without side effects.

Table 4.4 Lactulose Excretion, Mannitol Excretion and Lactulose/Mannitol Ratio in Patients with Seborrheic Dermatitis.

Patiet	Sex	Age	Lactulose excretion (%)	Mannitol excretion (%)	Lactulose/Mannitol Excretion ratio
M.M.	M	39	0.39	23.67	0.016
W.V.	M	43	0.37	20.88	0.018
S.L.	M	51	0.41	24.82	0.017
K.C.	M	43	0.38	19.87	0.019
W.C.	M	30	0.37	27.58	0.018
T.R.	F	29	0.46	20.80	0.022
A.K	F	47	0.35	23.45	0.015
A.A.	F	30	0.58	20.76	0.027
S.T.	M	48	0.59	21.60	0.027
T.N.	M	57	0.44	23.84	0.018
L.T.	F	37	0.56	20.80	0.027
P.T	M	30	0.44	23.80	0.018
P.J.	M	27	0.58	25.14	0.023
Pi.T.	M	34	0.42	24.18	0.017
J.B.	F	38	0.64	20.51	0.031
S.S.	F	41	0.44	22.36	0.020

Table 4.4 reports lactulose excretion, mannitol excretion, and L/M ratio in each patient with seborrheic dermatitis. All of patients with seborrheic dermatitis had increased lactulose excretion (normal range is 0.0-0.3%). Out of 16 patients, 2 patients had increased mannitol excretion (normal range is 9.5-25%). One patients with seborrheic dermatitis had L/M ratio outside the normal range (normal ratio is 0.00-0.03)

Table 4.5 Lactulose Excretion, Mannitol Excretion and Lactulose/Mannitol Ratio in Healthy Control Subjects.

Controls	Sex	Age	Lactulose excretion (%)	Mannitol excretion (%)	Lactulose/Mannitol Excretion Ratio
J.K.	M	30	0.25	20.51	0.012
N.P.	F	37	0.30	22.93	0.013
N.M.	F	53	0.25	22.84	0.011
P.D.	F	27	0.30	18.46	0.016
S.K.	F	60	0.30	23.88	0.013
S.S.	F	44	0.26	25.12	0.010
T.P	F	42	0.25	24.18	0.010
V.T.	F	29	0.26	21.56	0.010
W.S.	M	36	0.41	25.19	0.016
S.A.	M	31	0.46	20.81	0.022
S.H.	M	45	0.25	20.83	0.012
M.A.	F	35	0.28	20.71	0.014
J.P.	F	44	0.29	25.44	0.011
C.K.	F	29	0.25	22.83	0.011
P.M.	M	35	0.28	20.69	0.014
S.P.	F	30	0.23	22.20	0.010

Table 4.5 reports lactulose excretion, mannitol excretion, and L/M ratio in each healthy control subjects. Out of 16 healthy controls, only 2 subjects had increased lactulose excretion

(normal range is 0.0-0.3%), whereas other 14 subjects had normal lactulose excretion. In addition, out of 16 controls, 3 patients had increased mannitol excretion (normal range is 9.5-25%). None of patients with seborrheic dermatitis had L/M ratio outside the normal range (normal ratio is 0.00-0.03)

Table 4.6 Lactulose Excretion, Mannitol Excretion and Lactulose/Mannitol Ratio (mean ± SD) in Patients with Seborrheic Dermatitis and in Healthy Controls.

	Patients	**Controls**	**Mean Difference**	**p-value**
Mannitol excretion %	22.75±2.14	22.39±2.02	0.368	0.621
Lactulose excretion %	0.46±0.09	0.29±0.06	0.175	<0.001
L/M ratio	0.021±0.005	0.013±0.003	0.008	<0.001

Note. Patients and controls were compared using independent T-test. P value < 0.001 denotes very significant difference of lactulose excretion and L/M ratio.

Mannitol : There was no significant difference between mean mannitol excretion in paitents with seborrheic dermatitis (mean 22.75 ± 2.14) and the healthy control subjects (mean 22.39 ± 2.02) (p = 0.621) (Table 4.6). The mean difference between two groups was 0.368. The difference in mannitol excretion between patients with seborrheic dermatitis and healthy controls did not reach significance. (Figure 4.1)

Lactulose : The mean lactulose excretion in the patients with seborrheic dermatitis (mean 0.46 ± 0.09) was significantly higher than that of the healthy control subjects (mean 0.29 ± 0.06) (p < 0.001) (Table 4.6). The mean difference between two groups was 0.175. The difference in lactulose excretion between patients with seborrheic dermatitis and healthy controls reached significance. (Figure 4.1)

Lactulose/mannitol excretion ratios (L/M Ratio) : L/M ratio in the patients with seborrheic dermatitis, range 0.015-0.031 (mean 0.021 ± 0.005) were significantly higher than those of the healthy control subjects, range 0.010-0.022 (mean 0.013 ± 0.003) (p < 0.001) (Table

4.6). One patients with seborrheic dermatitis had L/M ratio outside the normal range. (normal range 0.00-0.03). (Figure 4.2).

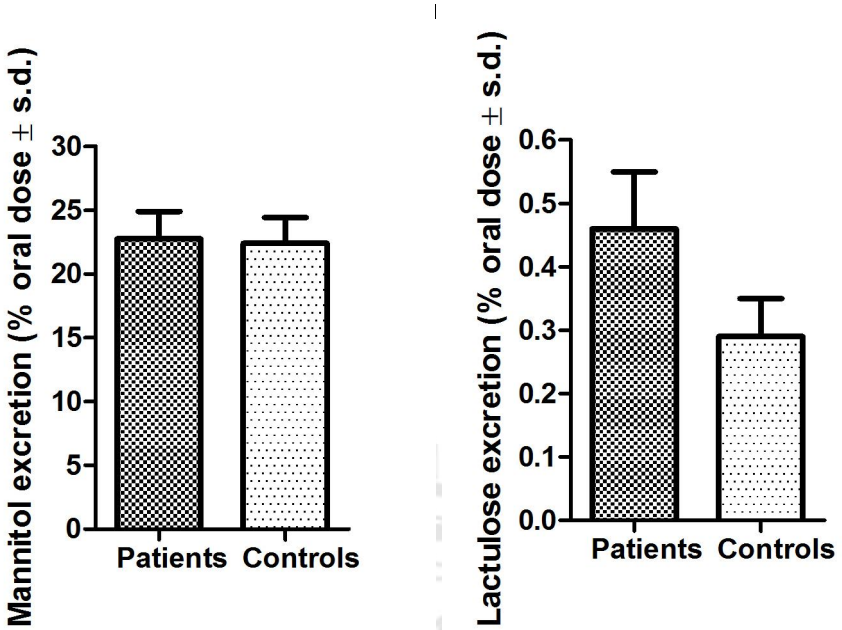


Figure 4.1 Mannitol and lactulose Excretion in Healthy Controls and in Patients with Seborrheic Dermatitis.

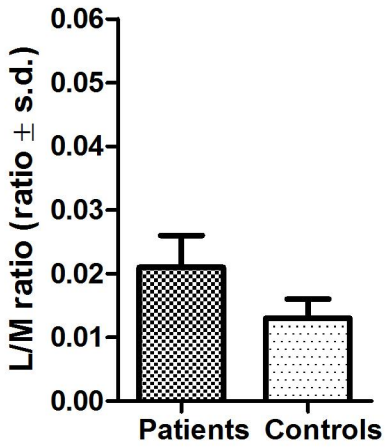


Figure 4.2 L/M ratio in Healthy Controls and in Patients with Seborrheic Dermatitis.

Table 4.7 L/M Ratio and Severity of Seborrheic Dermatitis in Patients with Seborrheic Dermatitis.

Patient	Sex	Age	Seborrhea Area Severity Index (SASI) (Maximum Score = 48)	Lactulose/Mannitol Excretion Ratio
M.M.	M	39	23	0.016
W.V.	M	43	36	0.018
S.L.	M	51	21	0.017
K.C.	M	43	24	0.019
W.C.	M	30	33	0.018
T.R.	F	29	28	0.022
A.K	F	47	13	0.015
A.A.	F	30	13	0.027
S.T.	M	48	16	0.027
T.N.	M	57	16	0.018
L.T.	F	37	4.5	0.027
P.T.	M	30	4.5	0.018
P.J.	M	27	8.5	0.023
Pi.T.	M	34	28	0.017
J.B.	F	38	30	0.031
S.S.	F	41	11	0.020

Table 4.8 Correlation between Severity of Seborrheic Dermatitis (Using Seborrhea Area Severity Index; SASI) and Lactulose Excretion, L/M Ratio in Patients.

	R	**p-value**
Lactulose excretion %	-0.328	0.215
L/M ratio	-0.156	0.563

Note. The correlation for parametric variables was analyzed by using Pearson test.

No increase of lactulose excretion and L/M ratio with the increase of severity of seborrheic dermatitis evident (Table 4.7). The rank correlation test for parametric variables (Pearson test), applied to data arrange in Table 4.8, shows a non-significant between the seborrhea area severity index (SASI) and lactulose excretion ($p = 0.215$). In the meanwhile, there was no correlation between SASI and L/M ratio ($p = 0.563$).

CHAPTER 5

CONCLUSION, DISCUSSION AND COMMENT

5.1 Conclusions

Sixteen healthy volunteers and sixteen patients with a diagnosis of seborrheic dermatitis were recruited from the outpatient department (OPD), Mae Fah Luang University Hospital and by local advertisement. The diagnosis of seborhheic dermatitis is based on clinical features by dermatologist. There is still no laboratory test or definite marker for establishing the diagnosis of seborrheic dermatitis. Clinical evaluation is the most important.

Initially, the hypothesis of this study states that there is a correlation between seborrheic dermatitis and increased intestinal permeability (leaky gut) that was measured by means of lactulose and mannitol test.

After the statistical analysis of the data obtained from 16 randomized patients with seborrheic dermatitis and 16 healthy control subjects; the results yielded a significant finding. In other words, the results obtained from the data support the original hypothesis.

5.2 Discussion

5.2.1 Demography

5.2.1.1 Sex: There were relatively more males in patient group than in the healthy control group. In general, seborrheic dermatitis can affect both males and females but it is much more common in men than women, probably because sebaceous gland activity is under androgen control.

5.2.1.2 Age: In the study, the mean age of patients with seborrheic dermatitis was 39 ± 8.82 years that was similar to the incidence. Seborrheic dermatitis has two age peaks, one in infancy within the first 3 months of life and the second around the third and fourth decade of life.

5.2.1.3 Underlying disease: Only one patient had Hepatitis B and the remaining 15 patients did not have any other underlying diseases. There was no underlying disease in all of healthy control subjects. There was no difference significantly in underlying disease between patients with seborrehic dermatitis and healthy controls. Therefore it was not an obstacle to the study.

5.2.1.4 Occupation: Most of healthy control subjects and patients were officers and doctors respectively. Because they were recruited from Mae Fah Luang university officers.

5.2.1.5 Signs and symptoms: The most severe symptoms were erythema followed by scaling and pruritus consecutively.

5.2.1.6 Affected areas: The most commonly affected area were the scalp followed by glabella or eyebrows and ears. More than one area could be affected in the same patient. Generally, the lesions favor scalp, face and ears.

5.2.1.7 Factors that trigger outbreaks: Both of the stress and inadequate sleep were the most common factor followed by dairy product consumption, followed by colder climate or exposure to air conditioning and exposure to the intense sunlight or heat.

5.2.1.8 Frequency of outbreaks: The most common frequency of outbreaks was 3-4 times a month.

5.2.1.9 Severity index: By using Seborrhea Area Severity index (SASI), The mean score of severity index was 18.8 out of 48. The severity of seborrheic dermatitis in patients was mild to moderate.

5.2.2 Intestinal permeability test

This method was chosen because it can be performed easily and non-invasive. By combining a small oral dose of lactulose and mannitol and then assessing for urine excretion, an intestinal permeability test quantifies malabsorption and leaky gut. The advantage of this method is that it is the most common test used for intestinal permeability studies. In addition, lactulose and mannitol meet most of the criteria for an ideal test substance. The degree of leak can be

assessed by ingesting lactulose and measuring for its presence in the urine. Lactulose is the large molecule and should not be absorbed or excreted through urine. Under leaky gut condition, it is absorbed through paracellular pathway and present in urine. On the other hand, mannitol is absorbed across the healthy mucosa and should be found in the urine, when ingested.

The result showed one of the sixteen patients had L/M ratio greater than the normal range. Although only one of 16 patients had L/M ratio outside the normal range whereas the other patients had L/M ratio within the normal range, patients with seborrheic dermatitis had L/M ratio higher than the normal healthy controls significantly. In addition, all patients with seborrheic dermatitis had increased lactulose excretion in urine indicating an abnormality of passive permeability (paracellular pathway) of small intestine. The increased lactulose absorption, indicating that the mucosa of the patients was more leaky than normal. On the contrary, mannitol absorption was normal that reflects small intestinal surface area was normal.

Immune cell function in seborrheic dermatitis is defective and it has been proposed that this defect contributes to the pathophysiology of seborrheic dermatitis. It may speculate that a leaky gut barrier in patients may facilitate specific immunological responses to cause disease. These is evidence that the restoration of normal intestinal permeability may improve disease. For example, in children with atopic dermatitis, probiotics treatment normalizes intestinal permeability and reduces eczema severity

Seborrheic dermatitis is considered as one of the endogenous eczema as well as atopic dermatitis but no data on increased intestinal permeabilithy in patients with seborrheic dermatitis can be found. Many works on increased intestinal permeability in patients with atopic eczema are available. There were atopic dermatitis has been reported associated with increased intestinal permeability. Baseline intestinal permeability measurements of children with eczema are higher than normal individuals. (Caffarelli et al., 1993; Pike et al., 1986; Przybilla & Ring, 1990; Rosenfeldt et al., 2004; Ukabam et al., 1984). Accordingly, the demonstration of increased excretion of lactulose in atopic dermatitis (AD) would indicate a leaky mucosa. This finding supports the hypothesis of the correlation between seborrheic dermatitis and leaky gut.

There was a negative correlation between the L/M ratio and the clinical severity of seborrheic dermatitis because not only increased intestinal permeability affects the severity of it, but also other factors that influence in the severity of seborrheic dermatitis. Several factors that

may influence in the severity such as stress, inadequate sleep, cold weather, sunlight and heat. Thus, the study has limitation because it is difficult to control factors that affect the severity of disease. However, in other clinical conditions, which are known to be associated with increase IP, and where IP is considered of pathophysiological relevance, such as irritable bowel syndrome, no correlation between the degree of IP and disease severity. (Zhou, Zhang & Verne, 2009).

5.3 Comments

The summary from this study will support that seborrheic dermatitis develop associated with increased intestinal permeability. Both pathophysiological and therapeutic implication of such an increased intestinal permeability in seborrheic dermatitis await for further studies. For example, the application for therapy directed toward reversing the increased intestinal permeability is logical such as elimination the causative factors, digestive enzyme replacement, reintroduction of friendly bacteria or probiotics (oral bacteriotherapy) , and providing nutritional support for regeneration or healing of the intestinal mucosa.

The study has the limitation. In the study, laboratory test or definite marker to confirm the diagnosis of seborrheic dermatitis were not performed especially skin biopsies to confirm the diagnosis precisely. Skin biopsies may effectively distinguish seborrheic dermatitis from similar disorders such as psoriasis, rosacea, and superficial fungal infection. Histological findings of seborrheic dermatitis are hyperkeratosis, acnathosis, accentuated rete ridges, focal spongiosis, and parekeratosis are characteristic. Psoriasis is distinguished by thin rete ridges, exocytosis, parakeratosis and an absence of spongiosis. Fungal culture can be used to rule out tinea capitis. The skin biopsies were not performed because it is an invasive technique.

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APPENDIXES

APPENDIX A

CONSENT FORM

หนังสือยินยอมเข้าร่วมโครงการวิจัย

หนังสือยินยอมในการเป็นผู้เข้าร่วมงานวิจัย

ข้าพเจ้า.....อายุ.....ปี

อยู่บ้านเลขที่ .....หมู่ที่.....ซอย.....ถนน.....

แขวง/ตำบล.....เขต/อำเภอ.....

จังหวัด.....

เบอร์โทรติดต่อ.....E-mail.....

ขอทำหนังสือนี้ไว้ต่อแพทย์ผู้รับผิดชอบครงการวิจัยเพื่อเป็นหลักฐาน

จุดประสงค์และภูมิหลัง

นพ.ไพศิษฐ์ ตระกูลก้องสมุท และโรงพยาบาลมหาวิทยาลัยแม่ฟ้าหลวง กรุงเทพมหานคร กำลังทำการศึกษาเพื่อประเมินความสัมพันธ์ระหว่างภาวะผนังลำไส้รั่วกับผื่นผิวหนังอักเสบเซบเดิร์ม โดยจุดประสงค์ของการศึกษาเพื่อพิจารณาว่า ผื่นผิวหนังอักเสบเซบเดิร์ม มีความสัมพันธ์กับภาวะผนังลำไส้รั่วหรือไม่ และผลการวิจัยจะได้เป็นแนวทางในการป้องกันและรักษาผื่นผิวหนังอักเสบเซบเดิร์มในอนาคต เนื่องจากในปัจจุบันสาเหตุของผื่นผิวหนังอักเสบเซบเดิร์มยังไม่เป็นที่ทราบแน่จัด จะมีผู้เข้าร่วมทดลองในการศึกษานี้ทั้งหมด 32 คน เป็นประชาการในประเทศไทยที่เข้ารับการตรวจที่โรงพยาบาลมหาวิทยาลัยแม่ฟ้าหลวง กรุงเทพมหานคร

หากข้าพเจ้าตกลงเข้าร่วมการศึกษานี้ สิ่งดังต่อไปนี้จะเกิดขึ้น

1. ข้าพเจ้าจะได้รับคัดเลือกเพื่อดูว่าข้าพเจ้ามีคุณสมบัติเหมาะสมสำหรับการศึกษาหรือไม่

2. ข้าพเจ้าจะได้รับการสอบถามข้อมูลเบื้องต้น กรอกแบบสอบถาม ตรวจร่างกาย ซักประวัติจากแพทย์ผู้รับผิดชอบการศึกษา

3. ข้าพเจ้าจะได้รับชุดตรวจดูการดูดซึมของผนังลำไส้ ประกอบด้วยขวดพลาสติกสีน้ำตาล บรรจุน้ำตาลแมนนิทอล 1.5 กรัม น้ำตาลแลคตูโลส 2.5 กรัม จำนวน 1 ขวด, ถุงพับขนาด 4 ลิตร สำหรับเก็บตัวอย่างปัสสาวะนาน 6 ชั่วโมง (ภายในใส่น้ำยา Chlorhexidine) จำนวน 1 ใบ

4. ข้าพเจ้าได้รับคำอธิบายวิธีการเก็บตัวอย่างปัสสาวะเพื่อส่งตรวจ โดยการรับประทานน้ำตาลแลคตูโลสและแมนนิทอล แล้วเก็บตัวอย่างปัสสาวะหลังรับประทานนาน 6 ชั่วโมงโดยแพทย์ผู้รับผิดชอบการศึกษา

5. ข้าพเจ้าจะไม่รับประทานน้ำผลไม้ ผลไม้ หลังรับประทานน้ำตาลแลคตูโลสและซูโครส นาน 6 ชั่วโมง

6. ข้าพเจ้าจะได้รับการบอกกล่าวถึงการค้นพบใหม่ๆ ในระหว่างการศึกษาวิจัยนี้ ที่มีผลเกี่ยวพันกับความสมัครใจในการร่วมการศึกษาวิจัยต่อไป

ความเสี่ยงและอาการไม่สบาย

ข้าพเจ้าจะแจ้งให้แพทย์ทราบทันที ถ้ามีผลข้างเคียงจากการรับประทานน้ำตาลแลคตูโลสและแมนนิทอล ได้แก่ คลื่นไส้ อาเจียน ปวดท้อง ท้องอืด ถ่ายเหลว แพทย์ของข้าพเจ้าจะให้การรักษาผลข้างเคียงที่อาจเกิดขึ้น ถึงแม้จะเป็นเวลานอกตารางการนัด ข้าพเจ้าสามารถติดต่อแพทย์ของข้าพเจ้าได้ตลอดเวลาในกรณีฉุกเฉินได้ที่ นพ.ไพศิษฐ์ ตระกูลก้องสมุท 089-4140943

ความเสี่ยงทางการเงิน

ข้าพเจ้าไม่ต้องเสียค่าใช้จ่ายเกี่ยวกับการตรวจดูการดูดซึมของผนังลำไส้เล็ก

ผลประโยชน์

ข้าพเจ้าจะทราบผลการตรวจปัสสาวะของข้าพเจ้าที่เกี่ยวข้องกับภาวะการดูดซึมของผนังลำไส้เล็ก

ทางเลือก

ข้าพเจ้าอาจเลือกปฏิเสธการตรวจ และออกจากการวิจัยได้ หรือปรึกษาแพทย์เฉพาะทางผิวหนังเกี่ยวกับการรักษาผื่นผิวหนังอักเสบเซบเดิร์มได้ โดยจะไม่มีผลกระทบต่อการรักษาทางการแพทย์ใดๆ ภายหลัง

หากข้าพเจ้าไม่ปฏิบัติตามข้อตกลง เช่น ไม่ให้ความร่วมมือในการเก็บปัสสาวะส่งตรวจ ข้าพเจ้าอาจถูกเพิกถอนจากการศึกษาวิจัยได้ แพทย์ของข้าพเจ้าสามารถร้องขอให้ข้าพเจ้าออกจากการวิจัยได้ โดยไม่ต้องแจ้งเหตุผลแก่ข้าพเจ้า

ค่าทดแทน

ข้าพเจ้าจะได้รับค่าตอบแทนสำหรับการร่วมศึกษาครั้งนี้เมื่อสิ้นสุดโครงการ เป็นจำนวนเงิน 100 บาท

คำถาม

แพทย์ที่ได้ลงนามท้ายนี้ได้พูดคุยกับข้าพเจ้าเกี่ยวกับการศึกษานี้ และข้าพเจ้าได้รับโอกาสในการถามคำถาม ข้าพเจ้าเข้าใจถึงความเกี่ยวข้องที่จะเข้าร่วมในการศึกษาวิจัยนี้ หากข้าพเจ้ามีคำถามอื่นเพิ่มเติมเกี่ยวกับการวิจัยนี้ ข้าพเจ้าจะติดต่อ นพ.ไพศิษฐ์ ตระกูลก้องสมุท ที่ 089-4140943 หรือ email : num_phaisit@hotmail.com

การปกปิดความลับ

ข้อมูลการเข้าร่วมการวิจัยของข้าพเจ้าจะถูกปกปิดเป็นความลับ ความเป็นส่วนบุคคลจะไม่ถูกเปิดเผยในรายงานใดหรืองานตีพิมพ์ใดที่เกี่ยวกับผลงานนี้ แพทย์ผู้วิจัยอาจทบทวนข้อมูลเกี่ยวกับข้าพเจ้าเพื่อตรวจสอบการศึกษาความถูกต้องของวิธีการดำเนินวิจัยทางคลินิก และ/หรือข้อมูลอื่นๆ โดยไม่ละเมิดสิทธิของข้าพเจ้าในการรักษาความลับเกินขอบเขตที่กฎหมายอนุญาตไว้ โดยข้าพเจ้าได้ลงนามในเอกสารใบยินยอมอนุญาตให้บุคคลต่างๆ ข้างต้นมีสิทธิตรวจสอบเวชระเบียนของข้าพเจ้าโดยตรง

หากข้าพเจ้าได้รับการปฏิบัติไม่ตรงตามที่ระบุไว้ในเอกสารชี้แจ้งผู้เข้าร่วมการวิจัย ข้าพเจ้าสามารถติดต่อกับประธานคณะกรรมการจริยธรรมสำหรับการพิจารณาโครงการวิจัยที่ทำในมนุษย์หรือผู้แทนได้ที่ ฝ่ายวิจัย สำนักวิชาเวชศาสตร์ชะลอวัยและฟื้นฟูสุขภาพ มหาวิทยาลัยแม่ฟ้าหลวง โทร 02-6642295-6

การยินยอม

การเข้าร่วมในงานวิจัยเป็นไปตามความสมัครใจของข้าพเจ้า ข้าพเจ้ามีสิทธิ์ที่จะถอนตัวจากการศึกษา ณ เวลาใด และการเพิกถอนดังกล่าวจะไม่มีผลต่อการดูลรักษาทางการแพทย์ของข้าพเจ้าในอนาคต การเข้าร่วมของข้าพเจ้าอาจสิ้นสุดเวลาใดก็ได้ ด้วยหรือไม่ด้วยความสมัครใจของข้าพเจ้า หากต้องการเข้าร่วมข้าพเจ้าจะลงชื่อข้างล่างนี้ ข้าพเจ้าจะได้รับสำเนาที่ลงชื่อเอกสารนี้เพื่อเก็บรักษาไว้

....

ลายมือชื่อผู้เข้าร่วมงานวิจัย วันที่

....

ลายมือชื่อแพทย์ผู้ขอคำยินยอม วันที่

ลงชื่อ .....

(.....)

หัวหน้าโครงการ

APPENDIX B

DATA COLLECTION FORM

แบบสอบถาม (สำหรับผู้ป่วย)

เลขที่แบบบันทึกข้อมูล.....

วันเดือนปีที่เก็บข้อมูล.....

1.ข้อมูลทั่วไปของผู้ป่วย

ชื่อ.....อายุ.....ปี เลขที่โรงพยาบาล.....

ที่อยู่….....

เบอร์โทรศัพท์ติดต่อ ..... มือถือ..... อีเมล.....

เพศ O ชาย O หญิง

อาชีพ O ข้าราชการ/รัฐวิสาหกิจ O พนักงาน O แม่บ้าน

O นักเรียน/นักศึกษา O กิจการส่วนตัว O อื่นๆ ระบุ.....

โรคประจำตัว O ไม่มี O มี ระบุ.....

ยาที่รับประทานอยู่เป็นประจำ O ไม่มี O มี ระบุ.....

สูบบุหรี่ O สูบ O ไม่สูบ

ดื่มแอลกอฮอล์ O ดื่ม O ไม่เดิม

2. ท่านมีอาการของโรคซีบอเรอิคเดอมาไตติส (เซ็บเดิม) เป็นประจำหรือไม่

O ไม่เป็น

O เป็น ระบุ ……ครั้งต่อเดือน

3. ท่านเคยเข้ารับการรักษาโรคซีบอเรอิคเดอมาไตติส (เซ็บเดิม) มาก่อนหน้านี้หรือไม่

O ไม่เคย

O เคย การรักษาที่ท่านเคยได้รับครั้งสุดท้าย

O ยาทา ได้รับครั้งสุดท้าย.....เดือน ชนิดยา.....

O ยารับประทาน ได้รับครั้งสุดท้าย.....เดือน ชนิดยา.....

4. ท่านสังเกตว่าโรคซีบอเรอิคเดอมาไตติส (เซ็บเดิม) มีอาการกลับเป็นซ้ำหรือกำเริบเมื่อ(ตอบได้มากกว่า 1 ข้อ

O พักผ่อนน้อย O เครียด O ทานผลิตภัณฑ์จากนมนม

O อาการเย็น/ฤดูหนาว O แสงแดดจัด/ความร้อน O ดื่มแอลกอฮอล์

O อื่นๆ ระบุ.....

5. อาการที่นำท่านมาพบแพทย์ (ตอบได้มากกว่า 1 ข้อ)

O แดง O คัน

O บวม O สะเก็ดขุยลอก

O แสบ O อื่นๆระบุ.....

แบบบันทึกข้อมูลวิจัยโดยแพทย์

แบบประเมิน Severity Index of Seborrheic Dermatitis (SASI Score)

เลขที่แบบบันทึกข้อมูล.....

วันเดือนปีที่เก็บข้อมูล.....

1. ชื่อ..... เลขที่โรงพยาบาล.....

2. ตำแหน่งที่พบรอยโรค

หว่างคิ้ว/คิ้ว	ร่องแก้ม	จมูก	ใบหู	หนังศีรษะ	อื่นๆ

หมายเหตุ ทำเครื่องหมาย X ในตำแหน่งที่มีรอยโรค

3. ความรุนแรงของแต่ละอาการที่หน้า

	Score = 0-4				
Erythema Face (EF)	None (0)	Very Mild (1)	Mild (2)	Moderate (3)	Severe (4)
Scaling Face (SF)	None (0)	Very Mild (1)	Mild (2)	Moderate (3)	Severe (4)

3. ความรุนแรงของแต่ละอาการที่หนังศีรษะ

	Score = 0-4				
Erythema Scalp (ES)	None (0)	Very Mild (1)	Mild (2)	Moderate (3)	Severe (4)
Scaling Scalp (SS)	None (0)	Very Mild (1)	Mild (2)	Moderate (3)	Severe (4)

3. พื้นที่ของรอยโรค

Degree of Involvement	Rating
<1%	0
1-10 %	1
11-20 %	2
21-35%	3
36-50%	4
51-75%	5
76-100%	6

Score = 0-6							
Area of Face (AF)	0	1	2	3	4	5	6
Area of Scalp (AS)	0	1	2	3	4	5	6

หมายเหตุ ทำเครื่องหมาย X การให้คะแนนความรุนแรง

4. สรุประดับความรุนแรง

SASI = 0.5 (AF)(EF+SF) + 0.5 (AS)(ES+SS)

SASI = ……..(maximum score = 48)

APPENDIX C

INTESTINAL PERMEABILITY TEST INSTRUCTIONS

คำแนะนำในการเก็บตัวอย่างปัสสาวะ (Intestinal Permeability Test Instruction)

การดำเนินการ กรุณาอ่านคำแนะนำต่อไปนี้ การดำเนินการไม่ถูกต้อง อาจทำให้ผลที่ได้ผิดพลาดไม่ถูกต้อง

<u>อุปกรณ์ที่ใช้</u>

- แบบคำขอ (Request form) 1 ใบ
- ขวดพลาสติกสีน้ำตาล บรรจุ Mannitol 1.5g/Lactulose 2.5ml (สำหรับผู้ใหญ่) จำนวน 1 ขวด
- ถุงพับขนาด 4 ลิตร สำหรับเก็บตัวอย่างปัสสาวะนาน 6 ชั่วโมง (ภายในใส่น้ำยา Chlorhexidine) จำนวน 1 ใบ
- หลอดพลาสติก (ขนาด 10 ml มีฝาเกลียวปิด) 1 หลอด
- ตัวหยดพลาสติก (Plastic droppler) 1 อัน
- ถุงเก็บตัวอย่าง BioHazard 1 ใบ
- ซองเพื่อบรรจุตัวอย่าง

<u>สาระสำคัญ</u>

- ก่อนการดำเนินการ กรุณาตรวจเช็คตามคำแนะนำ การละเลยข้อควรระวังนี้ อาจทำให้ผลที่ได้คลาดเคลื่อนได้
- -ก่อนเริ่มเก็บตัวอย่าง (ราว 23.00 น.) งดอาหารและน้ำดื่ม

<u>สาระเพิ่มความปลอดภัย</u>

- ข้อควรระวัง : หลีกเลี่ยงการสัมผัสกับของเหลวในขวดที่ผิวหนังหรือดวงตา
- Lactolose อาจพบอาการแน่นท้อง
- Mannitol อาจพบอาการแน่นท้อง หรืออาการคลื่นไส้ มีพบน้อยมาก

<u>การเก็บตัวอย่างสิ่งส่งตรวจ</u>

1. ให้ถ่ายปัสสาวะในห้องน้ำจนหมด หลังตื่นนอน และก่อนทานอาหารเช้า
2. เทน้ำอุ่น ผสมกับของเหลว ในขวดพลาสติกสีน้ำตาล จนมีปริมาตรราว ¾ ของขวด ปิดฝาขวดให้แน่น และเขย่า ขวดเพื่อละลายผงสีขาว
3. ดื่มของเหลวจนหมด หากยังมีของเหลวติดค้างในขวด ให้ผสมน้ำอุ่นเพิ่ม แล้วดื่มจนหมด
4. จดบันทึกเวลาที่ดื่มของเหลวผสมนี้ ลงในแบบคำขอ และบนหลอดเก็บตัวอย่างปัสสาวะขนาด 10ml
5. เริ่มทำการ เก็บตัวอย่างปัสสาวะลงในถุงพับขนาด 4 ลิตร ในช่วง 6 ชั่วโมงต่อมา ภายหลังดื่มของเหลวนี้ให้ทานอาหารเช้า ปกติ แต่งดผลไม้ น้ำผลไม้
6. เก็บตัวอย่างปัสสาวะลงในถุงเก็บปัสสาวะ ปิดจุกแล้วเขย่าให้ทั่ว อ่านปริมาณปัสสาวะที่มาตราวัดข้างถุง
7. จดบันทึกปริมาณปัสสาวะลงในแบบคำขอ และหลอดเก็บตัวอย่างขนาด 10ml
8. ใช้ตัวหยดพลาสติก ถ่ายน้ำปัสสาวะ จำนวน 10ml ลงในหลอด 10ml ปิดฝาให้แน่น และบันทึกชื่อ วันที่ และเวลา
9. วางหลอดนี้ลงในซองแล้วปิดซอง

CURRICULUM VITAE

CURRICULUM VITAE

NAME	Mr. Phaisit Trakulkongsmut
DATE OF BIRTH	13 November 1981
ADDRESS	72 Soi Sukumvit 62/1, Sukhumvit Rd., Bangjak, Phrakhanong, Bangkok 10260

EDUCATIONAL BACKGROUND

2000-2005	Bachelor of Medicine Program (Doctor of Medicine, M.D.), Prince of Songkla University, Thailand.

WORK EXPERIENCE

2011-present	Full-time physician (Anti-aging and Regenerative Medicine specialist) at Life Center, Samitivej Sukhumvit Hospital. Bangkok, Thailand.
2010-present	Anti-aging physician, School of Anti-Aging and Regenerative Medicine, Mae Fah Luang University, Bangkok, Thailand.
2010	Guest speaker for seminar “How to Choose Healthy Food and Nutrition for Anti-Aging”, Hadyai Hospital, Songkhla, Thailand.
2009-present	Columnist of Holistic and Anti-aging meidicne (Change your life column) for Slim up magazine
2009-present	Guest speaker for anti-aging medicine and health on the national broad casting television channel 5, Health plus channel, Dr.TV channel.

CURRICULUM VITAE (continued)

WORK EXPERIENCE

2009-2010	Anti-aging physician, TSD advance medicine clinic
2009-2010	Consultant for The Slim up center.
2007-2008	Aesthetic physician, Pongsak Clinic.
2006-2007	Internship, Songklanagarind University Hospital, Hadyai, Songkla province,Thailand.
2005	Extern with excellent performance, Trang Principal Hospital, Trang province, Thailand.