CHAPTER I

1.1. Background

Acne Vulgaris is one of the most common dermatological condition which dermatologists have to treat. It mainly affect adolescent, though may present at any age. Although acne is not a life threatening condition, it has a substantial psychological impact, leaving both physical and emotional scars on those who suffer.The principal hallmarks of acne include follicular hyperproliferation and plugging, extensive formation of sebum, activity of Propionibacterium acnes, inflammation and hormones.[1]In recent years, due to better understanding of the pathogenesis of acne, new therapeutic modalities and combinations have been designed. In topical agents; benzoyl peroxide, antibiotics, retinoids, etc are the main therapy for acne vulgaris or they can be given in combinations. While systemic therapy includes isotretinoin, oral antibiotics such as macrolides and tetracyclines, hormone-based therapies can be separated into two broad categories: androgen synthesis inhibitors and androgen receptor antagonists. Estrogen and progesterone derivatives, are generally considered androgen synthesis inhibitors. Commonly known androgen receptor antagonists include agents such as spironolactone, flutamide, cyproterone acetate, and progestins.[2] Which therapy to use is depend on the need of patients and it has to be selected. Specially in hormone therapy we must be very careful cause the side effect of hormone therapy such as cardiovascular risk and cancer risk must be consider. To avoid or to minimize the side effect of hormone therapy and to get better

treatment for acne vulgaris, we would like to know the effectiveness of isoflavone for acne vulgaris therapy.

According to the Global Burden of Disease (GBD) study, acne vulgaris affects about 85% of young adults aged 12–25 years.[3] Acne consistently represents the top three most prevalent skin conditions in the general population, as found in large studies with in the UK, France, and the USA. Similar numbers are reported for young adults in various countries through out the world. Epidemiological studies have demonstrated a higher incidence of acne vulgaris in different ethnicities of color in samples collected from the population aged 10–70 years. Data collected from 1990 to 2010 GBD was analyzed. Exhibits a general upward trajectory for all regions except Sub-Saharan Africa, with a clear separation in both prevalence and rate of incline between traditionally more wealthy regions (Western Europe, high-income Asia Pacific, US, and Canada) and traditionally poorer regions (Sub-Saharan Africa, Oceania, Latin America, and Caribbean). Similar patterns are seen for incidence and rate of incline in the comparison of developing versus developed nations.

Many research had been done finding the benefit of isoflavone. Isoflavone have been proven to have benefit for cardiovaskular health by affecting the vascular tone through a combination of mechanisms including endothelial-dependent and endothelial independent vasodilator systems and inhibition of constrictor mechanisms. These processes involve both classical genomic as well as non-genomic mechanisms of action. Activation of nuclear ERs by isoflavones was found to increase expression of endothelial NO-synthase (eNOS), reduce

oxidative stress and increase NO bioavailability.[4] In postmenopausal women, consumption of isoflavones was found to be associated with reduction of breast cancer incidence, mammary gland density, and proliferation ability of mammary gland cells. These effects have been associated with the ability of isoflavones to increase serum SHBG concentration, there by reducing the bioavailability of sexual hormones in hormone-dependent tissues .[4] Moreover, in peripheral tissues, isoflavones inhibit enzymes involved in the processes of cell proliferation (e.g. tyrosine kinase) and reduce estradiol availability through the inhibitory effect on aromatase P450 . Similarly to estradiol, isoflavones pass through the blood-brain barrier. Consumption of large amounts of soybeans increased the concentration of isoflavones in basal parts of the hypothalamus, the hippocampus, the cerebellum, and the frontal cortex. This corresponds well with regional expression of ERβ, which bind isoflavones . In contrast to peripheral tissues, the activity of aromatase P450 in the brain seems to be unaffected by dietary isoflavones. Surprisingly, decreased activity of 5α-reductase in the hypothalamus and amygdala has been reported at low, but not at high isoflavones intake.

Pilosebaceous units possess all the steroid metabolizing enzymes needed to convert dehydroepiandrosterone to the most potent androgen, dihydrotestosterone (DHT), including 3b -hydroxsteroid dehydrogenase , and 5a -reductase (5a -R).[1]Soybean isoflavone has active components, they are genistein, daidzein and glycitein.[4] The role of soybean isoflavone in androgen metabolism is to restrict the enzyme 3ß-hydroxysteroid dehydrogenase (3ß-HSD), 17ß-hydroxysteroid dehydrogenase (17ß-HSD) and the enzyme 5a-reductase.[4]In the previous research

about the benefit of isoflavone has been found that with the dose of 160 mg of isoflavone will reduce the amount of sebum production, acne vulgaris lessions and the level of DHT.[5] In this continues research we would like to know which is the best way of isoflavone 160 mg will give the best result in therapy of acne vulgaris. The association between consumption of soybean isoflavone and acne vulgaris is not known yet, so a study on the influence of soybean isoflavone supplementation on women with acne vulgaris by investigating androgen hormone that has association with the amount of acne vulgaris lesion, then formulate the problem of whether oral or topical soybean isoflavone has influence on amount of sebum and DHT hormone in acne vulgaris.

1.2. Problem of Research

Will oral or topical isoflavone therapy decrease the amount of sebum, decrease the activity of DHT reseptor and will isoflavone change the histology of sebacea gland.

1.3. Purpose of the Research

1.3.1. General Purpose

In this research we would like to know the effectiveness different of isoflavone oral or topical for acne vulgaris therapy by measuring the amount of sebum, the activity of DHT reseptor and histology of sebacea gland.

1.3.2. Specific Purpose

1. To investigate what is the effect of oral or topical of 16 mg isoflavones therapy to decrease the amout of sebum
2. To investigate what is the effect of oral or topical of 16 mg isoflavones therapy to decrease the activity of dihydrotestosterone (DHT) reseptor
3. To investigate what is the effect of oral or topical of 16 mg isoflavones therapy that can change the histology of sebacea gland

1.4. Research Originality

This research has not been done before, in this research we try to find out the effectiveness differences between oral or topical soybean isoflavone for acne therapy and comparing with the gold standart therapy that has been used until now.

Name,Year	Title	Metode	Result
Puguh Riyanto,Prasetyowati Subchan and Rosa Lelyana 2015	Advantage of Soybean isoflavone as antiandrogen on acne vulgaris	The study design is true experimental clinical study using randomized pretest-posttest control group design. This study used dosage of 160 mgs soybean isoflavone for	Supplementation with 160 mg/day of soybean isoflavone can reduce total AV lesion as a result of decreased DHT

		treatment group and 0 mg for placebo group for 12 weeks,	level.
Puguh Riyanto and Rosa Lelyana, 2017	Soy Isoflavones Reduce Toll-like Receptor-2 Levels in Acne Vulgaris.	Randomized pre- and post-test control design, with 40 women, randomized into 2 groups: placebo and treatment. This study has done for 12 weeks.	The treatment of 160 mg/day soy isoflavones for 12 weeks in women with suffered AV lesions has proved a significant reduction in total AV lesions cause of the reduction in TLR-2 levels.
Puguh Riyanto 2017	Effect of Soy Isoflavones on the Improvement of Acne Vulgaris Severity by Reducing Tumor Necrosis Factor-a	In this study was a clinical study with randomized controled group pretest-posttest design. 40 patients	Treatment with soy isoflavones 160 mg / day for 12 weeks can improve the degree of AV

	Levels.	were randomized into 2 groups: soy isoflavones 160 mg/day and control. The duration of this study was 12 weeks	severity as a result of a decrease in TNF-α.
Koltun et al., 2008.	Efficacy and safety of 3 mg DRSP (yasmin)/20 mcg EE oral contraceptive administered in 24/4 regimen in the treatment of acne vulgaris: A randomized, double-blind, placebo-controlled trial.	Randomized double-blind placebo controlled trial.	COC group had 4.31 odds of clear/almost clear skin as assessed by investigators after six 28-day cycles compared with placebo (p = .001).
NIU Ben,WANG Ai-xia,LIANG Ning,GAO Jun 2012.	Efficacy Observation of Moxa Flavone on Experimental Acne.	To observe the influences of 60,30 mg • kg-1 moxa flavone on models of experimental rabbit ear keratinization,the	The experiments show that moxa flavone can cure acne through the

		influences of 60,30,15 mg • kg-1 moxa flavone on the models of the rat voix pedis engorgement and rats blood stasis syndrome.	experimental keratinization,the blood circulation activating,stasis eliminating,antiinflammatory action,immunosuppression and androgen depreciation.
Palli et al., 2013.	: A single-center, randomized double-blind, parallel-group study to examine the safety and efficacy of 3 mg DRSP/0.02 mg EE compared with placebo in the treatment of moderate truncal acne vulgaris	Randomized double-blind parallel-group study.	COC group experienced significantly greater reductions in noninflammatory and total acne count by week 24 compared with placebo (p = .02).

1.5. Benefit Of The Research

1.5.1. Scientific Benefit

From this research we can find out which is the best way of isoflavone (oral or topical) for acne vulgaris therapy. Isoflavone can reduce the amount of sebum, decrease the DHT reseptor activity and change the histology of sebacea gland.

1.5.2. Practical Benefit

The result of this research will give us knowledge about the benefit of oral and topical isoflavone in acne vulgaris therapy and what is the best way to be use. Isoflavone maybe one of the alternative therapy for acne vulgaris. This will help the community to seak therapy and to prevent acne vulgaris. And we can reduce or prevent the side effect of hormonal therapy in acne.