PHYTOESTROGEN IN SKIN AGEING: THE CASE OF LABISIA PUMILA

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1.0 Introduction

1.1 Labisia pumila – the traditional use

Labisia pumila is under Myrsinaceae family, locally known as Kacip Fatimah, is one of the herbs that has been widely applied by decoction in South East Asian communities for a variety of illnesses. It is an indigenous medicinal herb of Malaysia and sometimes also referred locally as Akar Fatimah, Selusoh Fatimah, Tadah Matahari, Rumput Siti Fatimah, Bunga Belangkas Hutan and Pokok Pinggang [1]. There are three types of Labisia pumila, i.e. Labisia pumila var. alata (LPva), Labisia pumila var. pumila (LPp) and Labisia pumila var. lanceolata (LPvl) [2]. Each variety commands a different use and traditionally, local healers tend to use Labisia pumila var. alata and Labisia pumila var. pumila [3]. This herb’s extract is prepared by boiling the roots, leaves or the whole plant with water and the extract is taken orally [4][5]. The decoction of the roots is also given to pregnant women between one or two months before delivery, as this is believed to induce and expedite labour [1]. It has been also widely used with a long history by women in Malaysia to treat post-partum illnesses, to assist contraction of the birth channel [1], shrink the uterus, improve menstrual cycle, and weight loss [2]. It was also reported that Labisia pumila can be used for delaying fertility and to regain body strength; while some other folkloric uses include treatment of flatulence, dysentery, dysmenorrhoea, gonorrhoea and “sickness in the bones”[1].Therefore Labisia pumila is known as the “queen of plants” of all Malaysian herbs [6].

1.2 Phytoestrogen – towards skin perfection

With such a massive research concentrated on identifying the presence of phytoestrogen in Labisia pumila, it is possible for this herb to have a potential towards skin perfection. Nowadays, women especially are obsessing with good skin care and a promising effect in skin care products. They are now more careful in the selection of beauty products and they are more attracted with the nature-based products compared with chemical-based-products. At present, traditional methods for skin care has been recognized by many around the world. Researchers are now actively looking for the advantages
available to the ingredients used in making herbal-based cosmetics.

Isoflavons and coumenstan are two categories in phytoestrogen. Isoflavons are the one that has been thoroughly studied which displays similarity to those in mammal estrogen molecules. Isoflavons can be found in soy beans, lentils and red clover. Genistein and daidecin are the most important isoflavones as their structures are similar to 17β-estradiol. This explains the estrogen effects of genistein and daidecin which involve the interaction of these substances with estrogen receptor [7].

In Asia, the nutrition contents in food intake with its large phytoestrogen content are thought to be the reason why Asian women rarely suffer from climacteric symptoms. The use of isoflavons which is significantly superior to the synthetic estrogen could be useful in skin beautification. When phytoestrogens are topically applied, they behave like estrogens which enhance proliferation of the epidermis, supporting collagen synthesis and reducing enzymatic collagen degradation [8].

The application of phytoestrogen in skin beautification has been used recently as the cosmetic ingredient in one of the skin care products known as Novadiol®. A controlled open European multicenter study examined the effect of a cosmeceutical preparation including isoflavone (Novadiol®) on 234 women: maximum age of 65 years, at least 3 years since menopause, no HRT or other substances affecting the skin aging process [8][9]. From this study, skin dryness and roughness were significantly improved at the treatment area as compared to untreated skin areas. Facial wrinkles were significantly reduced by 22% and skin looseness was significantly reduced by 24% [8].

The effect of phytoestrogen was actively observed in soy. In fact, the benefits of soy in skin health have been focused on the isoflavones towards skin aging. Isoflavons from soy has been reported to support skin health which may not be related to the antioxidant properties but through other mechanism. Sudel et al [10] demonstrated that in vitro treatment of human fibroblast with purified genistein increased collagen synthesis [11].

1.3 Labisia pumila - the presence of phytoestrogen

The specific usage towards women’s health has led to the fact that this herb has high phytoestrogenic activity, or phytoestrogen, a compound with almost similar chemical structure to women’s hormone, estrogen [1]. In theory, the phytoestrogen acts as an anti-estrogen agent by limiting estrogen receptors and impose a much weaker effect of estrogen compared with the actual hormone [12][13]. Furthermore, exhibition of estrogeic activity has been shown with the increased of uterine weight in ovariectomized and dihydrotestosterone-induced polycystic ovarian syndrome rats, post-treatment with Labisia pumila [14]. Labisia pumila also initiate lipolysis in adipose tissue which is a similar effect as reported for estrogen [15].

Phytoestrogen is also known to be responsible in abortion and contraception. It is believed that estrogen plays an important role in causing uterine contraction during later stages of pregnancy and labour [1]. This herb would be able to relieve menopausal symptoms [16]. Treatment with this herb maintained the elastic lamellae architecture of the ovariectomized rat aorta as compared to normal rats. The comparison of both Labisia pumila extract and estrogen replacement therapy showed Labisia pumila extracts could thicken aortic wall as compared to estrogen treatment. The benefit of having a more elastic aorta is to allow the smooth flow of blood from the heart without putting unnecessary stress on other organs [16]. These results are consistent with previous research which phytoestrogen intake was also reported to be involved with low aortic stiffness [17] thus it would be possible to apply the same concept to Labisia pumila, based on the estrogenic activity of the extract.

Few phytochemicals have been identified in Labisia pumila [18] such as anthocyanins, phenolic acids, and flavanoids [19]. These components are believed to be responsible for the wide spectrum of pharmacological activities attributed to the herb. It was reported that antioxidant activity from aqueous extract of this herb provides significant protection to human fibroblast, from cell damage caused by UV irradiation [20], most likely to the presents of these components. The roots and leaves of Labisia pumila were found containing two novel benzoquinind compounds 1,2 as major components [18].

A preliminary screening of total phenolic content (TPC) was done by Chua et al [21]. The study shows that MeOH extract of this herb contained the highest amount of phenolic phytochemicals, as compared to 60% MeOH extract. Flavonoids constituted a large portion of the phytochemicals in the 60% MeOH leaf extract. The 40% MeOH fraction was found to have the highest DPPH scavenging activity. Nine flavonols, two flavanols and nine phenolic acids were detected in this fraction using UPLC–ESI-MS/MS coupled with powerful software for data processing and interpretation [21].

It is believed that extracts of Labisia pumila have antioxidative properties comparable to Silymarin, an extract of the well-known European milk thistle plant Silybum marianum [22]. A study done by Norhaiza, Maziah and Hakiman [18] showed that varieties, L. pumila var. alata and L. pumila var. Pumila have high antioxidant activity. There is a positive correlation between antioxidant capacities and individual antioxidative compounds in the following order β-
Menopause is one major phase in women’s life which has been a big concern especially in skin modification. The skin is a target of many hormones, especially estrogens. Estrogen and other hormone receptors have been detected, in keratinocytes, fibroblast, sebaceous glands, hair follicles, endocrine glands, and blood vessel. This is one of the main reasons of postmenopausal women having aged skin – they are lacked of estrogens hormone. In clinical terms, many females experience a sudden onset of skin aging symptoms several months after menopause. Several studies showed that the lack of estrogens in the system is associated with aging effects, especially for women who experience menopause.

The first sign of menopause which women experience is increasing skin dryness followed by a loss of skin firmness and elasticity that lead to wrinkles. Every year, skin collagen content in adults will decrease 1% gradually and this process is more obvious to women than men. Approximately, nearly 30% of skin collagen will be lost in the first five years after menopause, with an average decline of 2.1% per postmenopausal year over a period of 20 years. However, with estrogens, this trend will be reversed and due to several pathways, the skin collagens increase and enhance the synthesis of hyaluronic acid and promote water retention hence correcting skin function and structure. Animal studies indicate that estrogen induce several changes in the connective tissue of the dermis, including increment of mucopolysachharide incorporation, hydroxyl-prolyn turnover and alterations in the extracellular matrix. Other studies has yet to be done for suitable candidate in combating aging skin towards these women and several hormone-based products have been tested to be positive in reducing aging effect.

1.4 The post-menopausal skin and estrogen

Aging is a continuous process from birth to the end of life. Menopause is one major phase in women’s life which has been a big concern especially in skin modification. The decrease in estrogen production is the hallmark of menopause which may be followed by gradual changes in menstrual cycle, accompanied by changes in gonadotrophine hormone with the increase of follicle stimulating hormone (FSH). The number of ovarian premature follicles is fixed at birth and gradually decreases each time follicles mature and release oocytes for reproduction. At certain stage, the follicular number has decreased substantially and responds poorly to FSH and LH, resulting in cycle irregularity and erratic ovulation. Hormone fluctuations are common at this stage, and there will be gradual decrease in progestrone and estrogen. This stage, which is called pre-menopause stage, will last from 3 to 10 years before menopause. Women will have irregular menstrual cycles as the first sign of pre-menopause along with increasing levels of FSH. Estrogen production continues to decrease due to the decreased number of follicles and leads to non-ovulatory cycles. At the onset of menopause, when ovulation ceased entirely, LH starts increasing again.

Ovarian steroidogenesis during menopause is restricted to androgen production. It is established that menopausal theca cells are responsive to LH and produce androstenedione and testosterone. Most of the circulating androgens come from the adrenal gland. During menopause, estrone is exclusively produced at remote sites (mainly adipose tissue) by the conversion of androstenedione. The rate of this conversion correlates to body size (amount of adipose tissue).
fibroblast and epidermal keratinocytes [34]. In a study to identify specific estrogen-sensitive structures, normal human skin was investigated for the binding of the ER D5 antibody which is associated with p29, a 29kD protein found in cytoplasm of normal estrogen-sensitive cells[35]. Strong and specific staining was seen in the epidermis, with a gradient showing the most intense staining in the granular layer. Similar positive staining was seen in the hair follicles and sebaceous glands. Variable staining was seen in the endocrine glands and vessels. These findings demonstrate the receptor p29 to be present in these structures, and hence suggest that estrogens may exert a specific effect on these tissues.

Estrogen could increase the rate of collagen production also influencing the degree of polymerization of GAG’s (glycosaminoglycans). Estrogens increase dermal hydroscopic qualities [36], probably through enhanced synthesis of dermal hyaluronic acid [37]. Collagenous fibrils were found to be less fragmented in the dermis in women treated with estrogens.

The decline in skin collagen content after the menopause occurs at a much more rapid rate in the initial postmenopausal years than in the later ones. Some 30% of skin collagen is lost in the first 5 years after the menopause with an average decline of 2.1% per postmenopausal year over a period of 20 years [38]. The increase in skin collagen content after 6 months of sex hormone therapy depends on the collagen content at the start of treatment [38]. In women with a low skin collagen content, estrogens are initially of therapeutic and later of prophylactic value only. Thus a deficiency in skin collagen can be corrected but not over corrected [39]. Following the menopause, skin collagen content and skin thickness are increased in women on estrogen replacement therapy compared to age matched women on no treatment [40][41]. Prospective studies have shown that skin thickness, skin collagen and bone mass increase in postmenopausal women who start estrogen replacement. Beneficial changes can be obtained using both topical [42] as well as oestradiol implants. Topical oestriadiol gel has also been shown to increase skin collagen content as measured by skin hydroxyproline. Skin blister fluids were assayed and an increase of both Procollagen C-End Terminal Pro Peptide (PICP) and Procollagen N-End Terminal Pro Peptide (PINP) characterized with the gel. Pro Collagen C-End Terminal polypeptide protein and Pro Collagen N-End Terminal polypeptide are released by enzymatic cleavage when the pro collagen molecule is released extracellularly. This is therefore a posttranslational event and the presence of free PICP and PINP serves to indicate collagen production. The ‘I’ in PICP and PINP refer to Type I Collagen.

A study done by Patriarca et al. [43] evaluates the additional benefits of topical estrogen on the dermal collagen of the facial skin in postmenopausal women using oral hormone therapy. Estrogen receptors have been detected in skin, and recent studies suggest that estrogens exert their effect in skin through the same molecular pathways used in other non-reproductive tissues. Although systemic menopausal hormone therapy (MHT) has been used for many years, recent trials have reported a significant increased risk of breast cancer and other pathologies with this treatment. This has led to reconsider the risks and benefits of MHT [44]. For this reason, high doses of systemic MHT cannot be recommended to treat skin aging. Therefore, the topical estrogen treatment may be an alternative for ameliorating the skin, specially the collagen amount. Patriarca et al. showed that the addition of estrogen gel may be useful for increasing the dermal collagen.

Patriarca et al. also suggests that topical estrogen could act on the skin without increasing its systemic level by the fact that topical estrogen may increase the collagen amount and prevent the cutaneous aging [45]. From this study, the systemic estrogen alone did not seem to have a positive effect in skin collagen. Otherwise, some studies showed that the decrease in skin collagen in women of postmenopausal age may not be an exclusive age-related phenomenon, but could be related to hypoestrogenism [41][43][46][47].

1.6 Labisia pumila – as a hormonal therapy towards skin aging

Based on the evidence shown in this paper, it is possible for this herb to be a hormonal therapy towards skin aging especially amongst premenopausal and post-menopausal women who are exposed directly towards skin aging. According to previous studies, this herb contains various kinds of phenolic compounds which demonstrated high antioxidant activity. There are very few researches conducted using this herb towards skin perfection and it was proved that this herb could protect skin cells from photo-aging caused by UVB irradiation. However, the important components of the plant such as phytoestrogen, also need to be taken into account due to the usage of this herb towards women’s health. It is possible that this herb has the same benefits as soy, which is rich in phytoestrogen. Soy has so much benefit towards women’s health and studies of this plant is already massively done by researchers. Phytoestrogen has been known by manyo have the ability to mimic the estrogen functionality and could bind estrogen receptors and had higher affinity for estrogen receptor β (ERβ) than ERα. Estrogen can be replaced by phytoestrogen especially in hormone replacement therapy that has been widely used for treatment in postmenopausal women. Hormone replacement therapy is a way of menopausal women to treat skin aging.
2.0 Discussion and Conclusion

*Labisia pumila* is a Malaysian traditional herb that has been a centre of popularity among all herbs in Malaysia after *Euricoma longifolia*. Although studies are more into *Labisia pumila* var. alata and *Labisia pumila* var. pumila, it is believed that other varieties of *Labisia* species have also possess a therapeutic value as those two. It is known amongst the traditional practitioners as queen of herbs and all the scientific knowledge from this herb is now being actively dug out by local researchers. It is interesting that this herb could be a possible candidate in replacing estrogenic drugs. Due to high phytoestrogen content in this herb, the potential to make it one of the key ingredients in the production of cosmetic products is very good, especially for women who suffer from premenopausal aging. As estrogen is one of the key factors in revitalizing women’s health, this herb is also useful in replacing synthetic drugs used in HRT. Estrogen is a type of hormone that is responsible for restoration of skin structure which is proof to be lacking in menopausal women. The mechanism of actions of the phytochemicals present in *Labisia pumila* might be similar to those demonstrated by estrogen. This herb also shows a great potential and might be equivalent to soy itself. Soy is one of the great sources of phytoestrogen and has been used widely in cosmeceutical products. As *Labisia pumila* is rich in antioxidant compound and shows phytoestrogenic properties, it can lead up to any research area especially in skin restoration therapy.

Acknowledgement

This review article was produced with the support from Universiti Teknologi Malaysia (UTM) Research University’s fund Q.J130000.7125.01H23 and facilities provided by Institute of Bioproduct Development (IBD), UTM.

References


