THE INFLUENCE OF SOY ISOFLAVON TO THE SKIN AGING IN PRE-MENOPAUSAL WOMEN

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SUMMARY

Skin aging process on pre-menopausal women is a problem that needs to be prevented as early as possible. The decrease of oestrogen level which is one of the intrinsic factors of the skin aging process will affect the skin biological process, due to oestrogen receptors on the skin. A number of researches conducted on pre-menopausal women with the allocation of oestrogen hormone resulted in delaying the skin aging process. The administration of soy isoflavon, a phytoestrogen found in daily food, on pre-menopausal women is hoped to be able to prevent skin aging process, even clinically or molecular biologically. This research aims to explain the benefit of administering of soy isoflavon on skin aging process.

The design of the research is randomised controlled trial (RCT). As many as 60 pre-menopausal women were collected with simple random sampling method. Soy isoflavon is an independent variable, while skin aging process is a dependent variable assessed from the hydration, sebum level, average roughness, depth of wrinkles, skin clarity, length of the telomere. Analysis was conducted using t and MANOVA tests and.the result showed a significance (F = 10,439; p = 0,001) over the allocation of soy isoflavon to the whole variable dependent, including the telomere length and the skin hydration, meant that allocation of soy isoflavon could delay skin aging process.

Introduction

The aging process on woman has its own effect due to the arrival of the women to the end of the reproduction period, namely climacterium period and senile period. Commonly climacterium period happens around the age of 40 – 65. At the beginning of their forties, women experience a decline of their ovarian's function which results in the decrease production of oestrogen hormone cyclically, together with the clinical effects which includes rough, dry, thin and wrinkly skin, and pigmentation spots. The decrease of the oestrogen level will affect the biological process on the skin, due to the presence of oestrogen receptors on the skin especially on the face and the back of the hands, as well as being one of the intrinsic factors of the true skin aging process.

The effects of oestrogen towards the skin are : (1) affects the mitosis of keratinocyte cells since it has an epidermopoetic nature, (2) affects fibroblast to synthesize collagen, elastin and the basic substance of macroprotein, (3) affects dermis vascularization which provides nutrition to the epidermis, (4) affects the production of the sebaceous gland to keep skin hydrated.

The changes on the skin that are connected to menopause are in accordance to the chronological skin aging process. The various changes can be pictured as morpholitic. The most obvious change occurs on the dermis, thus researches concerning on skin aging process has to be focused on cell playing a role on synthesis and maintaining extra cellular matrix. Fibroblast is the most abundant cell and most important one in maintaining skin metabolism.

The cell aging process is caused by the gradual loss of telomere. The skin cell has a limited ability to replicate, which will be obvious during the aging process. The length of the telomere can provide a picture of the ability of cell to replicate so it can be used as a milestone to the cell aging process.

Soy contains a phytochemical compound, called isoflavon, which has a similar activity like homoestrogen because it can interact with oestrogen receptor and is actually a weak oestrogen. The main component of isoflavon are genestin and daidzin which have the chemical structure similar to oestrogen in its aromatic ring A with two hydroxyl groups separated in 12,1 Å distance. This distance makes the phytoestrogen can bind the oestrogen receptor and give the similar respond like oestrogen, behave as agonist (=oestrogenic, the activity is in the same direction with oestrogen) and antagonist (=anti oestrogenic, the activity is in the contra direction with oestrogen). The only difference is that phytoestrogen is not a steroid and doesn't have any closed cyclopentane from aromatic benzene ring. In the abundance of oestrogen, phytoestrogen will bind the oestrogen receptor and makes a block towards stronger oestrogen molecule. On the other side, in the minimal amount of oestrogen like in menopause, phytoestrogen will predominantly bind oestrogen receptor, giving oestrogenic respond. People now tend to go 'back to nature' by using natural products, thus it is important to administer a natural alternative hormone replacement therapy with soy isoflavon for pre-menopausal woman to prevent, even alleviate the symptoms.

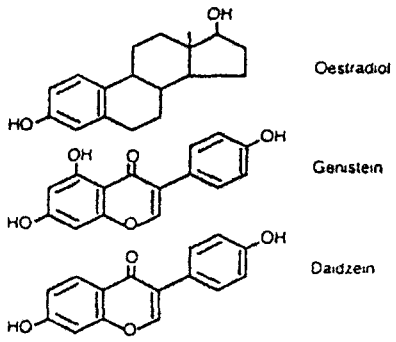

Figure 1 : The structures of oestrogen oestradiol, genestein and daidzein

Objective

This research aims to find out the benefit of administering soy isoflavon toward skin aging process on pre-menopausal women. The originality of this research lays on the study of molecular biology used as one of the skin aging process parameters.

Method

The research was conducted in the Out Patient's Department of Dermatology and Venereology, dr. Kariadi General Hospital, Semarang. The decision to choose the location in dr. Kariadi General Hospital is to allow the samples being considered as homogenous so the possibility of bias can be prevented. The research was conducted to prove the effects of isoflavon on the skin both by clinical and molecular biological tests with a double blind randomised research design done for 3 months.

The population target is pre-menopausal women and the research sample is the woman employees of dr Kariadi Hospital and General Hospital of Rumani in Semarang. As many as 60 women were collected with simple random sampling method and divided into two groups consisted of 30 women each. The first group were given 40 mg capsules of soy isoflavon as a treated group and the second were given 40 mg capsules placebo as a control group. The dispensing of the capsules was tightly controlled to assure the patient's compliance. These women administered two capsules after breakfast and two capsules after dinner for 12 weeks long.

Soy isoflavon acts as an exposure variable, while skin aging process as the effect variable assessed from level of hydration by Corneometer (CM 825 Courage & Khazaka), sebum level by Sebumeter (SM 810 Courage & Khazaka), roughness and

the depth of wrinkles by Skin Visiometer (SV 400 Courage & Khazaka), clarity by Mexameter (MX 16 Courage & Khazaka) and telomere length done by DNA isolation after 12 weeks administering of soy isoflavon. The history of previous using sunscreen, habit of exercise, temperature, air pollution, stress, and compliance would be assessed as bias variable. The analysis is done using t and Manova tests.

Result

The mean level of skin hydration in the beginning of the research was not statistically different (t=1,057; p=0.295), while the mean of skin hydration at the end and in the beginning of the research was very significantly different (t=4,364; p=0.001) showed a difference in the level of skin hydration between the two groups, meant that the administration of soy isoflavon increasing the skin hydration.

Table 1.

Level of Skin Hydration in the Beginning and the End of the Reseach

Group	Mean ± Std. Deviation		
	* The Beginning	** The End	*** Δ (Difference)
Treatment Group	92,07± 18,44	98,37 ± 16,88	6,30 ± 5,91
Control Group	86,67± 21,03	79,13 ± 18,90	-7,54 + 16,32

t test : * t =1.057, p=0,295
** t =4.158; p=0.001
*** t =4.364; p=0.001

The mean level of skin sebum in the beginning of the research in both groups were not statistically different (t= -0,197; p=0.845), and also at the end of the research, which was not statistically different (t=1,576; p=0,120) showed that there was no difference on skin sebum level between the two groups. In other words, the administration of soy isoflavon did not increase skin sebum level.

Table 2.

Level of Skin Sebum in the Beginning and the End of the Research

Group	Mean ± Std. Deviation		
	* The Beginning	** The End	*** Δ (Difference)
Treatment Group	48.20±33.32	56.07±31.70	7.87±26.49
Control Group	49.73±26.72	49.10±22.14	-0.63±13.05

t test : * t = -0.197; p=0.845
** t = 0.987; p=0.328
*** t =1.576; p=0.120

The mean of skin clarity of both groups in the beginning of the research was statistically similar (t= -1,206; p=0,233), also at the end of the research, where no difference was found statistically (t=1,272; p=0,209) showed no difference of skin clarity on the two groups, which meant that the administration of soy isoflavon did not increase skin clarity.

Table 3.

Skin Clarity in the Beginning and the End of the Research

Group	Mean ± Std. Deviation		
	* The Beginning	** The End	*** Δ (Difference)
Treatment Group	546.13 ±16.69	543.43±18.41	-2.700± 5.18
Control Group	551.97± 20.57	532.80 ±74.66	-19.17± 70.73

t test : * t= -1,206; p=0,233
** t=0.757; p=0.452
*** t=1.272; p=0.209

The mean of skin roughness on both groups in the beginning of the research was significantly and statistically different (t= -2.121; p=0,038), while the mean difference of skin roughness in the beginning and at the end of the research is not statistically different (t=0,674; p=0,503) between the two groups. It means that the administration of soy isoflavon did not affect the skin roughness.

Table 4.

Skin Roughness in the Beginning and the End of the Research

Group	Mean ± Std. Deviation		
	* The Beginning	** The End	*** Δ (Difference)
Treatment Group	0.1681± 0.0370	0.1617 ± 0.0291	-0.0064 ± 0.0318
Control Group	0.1956 ± 0.0606	0.1802 ± 0.0289	-0.0154 + 0.0652

t test : * t= -2.121; p=0.0318
** t= -2.480; p=0.016
*** t=0.674; p=0.503

The mean of the depth of the wrinkles on both groups in the beginning of the research was not significantly or statistically different (t= -0,900; p=0,372), while the mean difference of the wrinkles at the end and in the beginning of the research was not statistically different (t=0,747; p=0,458). It means that the administration of soy isoflavon did not affect the depth of the wrinkles.

Table 5.

The Depth of the Wrinkles in the Beginning and the End of the Research

Group	Mean ± Std. Deviation		
	* The Beginning	** The End	*** Δ (Difference)
Treatment Group	0.1312± 0.0374	0.1617±0.0290	0.0305± 0.1671
Control Group	0.1390± 0.0293	0.1802± 0.0232	0.0412± 0.0302

t test : * t= -0.900; p=0.372
** t= 0.541; p=0.590
*** t=0.747; p=0.458

The mean of telomere length between the two groups in the beginning of the research was not statistically different (t= -1,021; p=0,312), while the difference of the mean of the telomer length in the beginning and at the end of the research was statistically different (t=6,649; p=0.001), showed that there was a difference in the telomer's length in the two groups. In other words, the administration of soy isoflavon could maintain the length of the telomere.

Table 6.

Telomere Length in the Begining and the End of the Research

Group	Mean ± Std. Deviation		
	* The Beginning	** The End	*** Δ (Difference)
Treatment Group	6.0963±0.0782	6.0797±0.0772	-0.0166 ± 0.0129
Control Treatment	6.1210±0.1068	6.0710±0.1006	-0.0500 ± 0.0242

t test : * t= -1.021; p=0.312
** t=0.374; p=0.710
*** t=6.649; p=0.001

From the result of Manova assessment with the factors of the treated group and the control group, the dependent variable was the difference at the end and in the beginning of the research regarding skin hydration, skin sebum level, skin clarity, the mean of skin roughness, the depth of wrinkles and telomere's length turned out to be significant (F=10,439; p=0,001) toward the dependent variable simultaneously. So, the administration of soy isoflavon can delay skin aging process.

Table 7.

t Test in the Beginning and the End of the Research

			The Beginning				The End			
					t-test for equality of Means				t-test for equality of Means	
	Research Group	N	Mean	Std. Deviation	t	Sig. (2-tailed)	Mean	Std. Deviation	t	Sig. (2-tailed)
Skin Hydration	Treatment	30	92.07	18.44	1.057	0.295	98.37	16.88	4.364	0.001
	Control	30	86.67	21.03			79.31	18.90		
Level of Skin Sebum	Treatment	30	48.20	33.32	-0.197	0.845	56.07	31.70	1.576	0.120
	Control	30	49.73	26.72			49.10	22.14		
Skin Clarity	Treatment	30	546.13	16.69	-1.206	0.233	543.43	18.41	1.272	0.209
	Control	30	551.97	20.57			532.80	74.66		
Skin Roughness	Treatment	30	0.1681	0.0370	-2.121	0.038	0.1617	0.0291	0.674	0.503
	Control	30	0.19557	0.0606			0.1802	0.0289		
The Depth of the Wrinkles	Treatment	30	0.1312	0.0374	-0.900	0.372	0.1617	0.0290	0.747	0.458
	Control	30	0.13903	0.0293			0.1802	0.0232		
Telomere Length	Treatment	30	6.0963	0.0782	-1.021	0.312	6.0797	0.0772	6.649	0.001
	Control	30	6.121	0.107			6.0710	0.1006		

Discussion

The skin changes due to pre-menopause are in accordance with the chronological skin aging process. Hormonal factors have a strong relationship with age and the appearance of skin aging process physiologically. The signs of skin aging are dry, rough, less elastic skin, pigmentation spots and wrinkles.

Soy isoflavon has an effect similar to homoestrogen or can interact with oestrogen receptors. Several data show that by consuming a small amount of soy protein will give an effect similar to oestrogen hormone which its level in blood is relatively high, thus giving significant hormonal effect on pre-menopausal women.

Oestrogen can be metabolised actively in the skin by target cells that have a characteristic dependent to oestrogen. Oestrogen is always involved in the activity of epidermis and fibroblast cells, thus oestrogen deficiency can accelerate skin degeneration including atrophy of the epidermis, sebaceous cells, and decrease of dermal vascularization which is important for nutrition of the basic layer of the epidermis.

In the research it could be observed that there was a difference in the mean of skin hydration in the beginning and at the end of the research on the treated group as a result of administration of soy isoflavon, which is in accordance to the research conducted by Branco et al (1992). Soy isoflavon can bind Estrogen Receptor so it will support fibrocyte to produce glycosaminoglycan which is the main constituent of dermis due to the ability to retain water up to one thousand times of its content, although only 0.2% from skin's dry weight.

In this research the skin sebum level did not significantly different in those two groups. It means that the administration of soy isoflavon can not increase the skin sebum level because skin sebum production is not depend on oestrogen deficiency only. Moelyanto RD (1994) said that in age people we could expect certain damage on sebaceous gland due to the loss of cells that are connected to the aging process. The more the age, androgen and sebum production also decrease up to 60%, thus causing the skin to dry. Oestrogen only affects sebum production, while androgen stimulate the mitosis of sebaceous cells and increase sebum production, but with the increase of age, androgen hormone will decrease.

Oestrogen deficiency causes imbalance of the skin pigmentation both clinically and spectrophotometrically. Leonard Hayflick and Moor Head (1961) reported that the more the age, the ability to replicate fibroblast, keratinocyte and melanocyte would also decrease. There is also a change in melanin pigment distribution which affect the skin aging process as well as sunlight, environmental toxicity, hormone, etc. In this research the mean of the difference in both groups was not significantly different.

The administration of soy isoflavon giving a response similar to oestrogen, is expected to improve the distribution of melanin pigment. But the use of oral contraceptive which increase the melanocyte activity due to increasing the oestrogen level in melanocytes, causes a slowly skin hyperpigmentation and continues to develop with exposure to sunlight (Neil, Eves and Richardson, 2000).

The decrease of oestrogen also reduces collagen polymeration and synthesis that would accelerate collagen degradation. As a result, the decrease of these basic substance could lead to reduced skin thickness, as seen as dry, rough, wrinkly, scaly and loose skin.

In this research we did not find any significant difference in the skin roughness on both groups. This fact is not in accordance with the result of the research conducted by Branco et al (1992).

According to Olovnikov, the cell's aging process is caused by the gradual loss of telomere. Skin cell possesses a limited ability to replicate, seen during the aging process. The length of the telomere will picture the ability of the cell to replicate so it is used as a marker of cell's aging process. In this research, it was shown that there was a significant difference of the mean of the telomere length at the end and in the beginning of the research on the treated groups. This fact is in accordance with our previous research on human skin fibroblast culture with the administration of soy isoflavon exposure (genestein), without exposure and FCS exposure, resulting different telomere length which is longer in the group with exposure to soy isoflavon.

As a general result of the research we found a significant difference in the telomere length between two groups, meant that administering soy isoflavon will inhibit the replication of fibroblast cell, and slowing the skin aging process.

With the deceleration of skin aging process in pre-menopausal women and other benefits that can be reaped, the hormone replacement therapy with soy isoflavon can be utilized as an alternative therapy in the dermatology and venereology department, especially in the medical cosmetic sub-department.

Further research is still needed to understand better about the benefits and other effects and the dosage of soy isoflavon in the dermatology and venereology department, especially in the medical cosmetic sub-department.

It is advised to consume soy and its products to pre-menopausal women .

CONCLUSION

1 The administration of soy isoflavon could increase skin hydration ($p=0.001$), proving that skin aging process could be slowed down.

2. The administration of soy isoflavon could maintain telomere length ($p=0.001$), meant that soy isoflavon can slow skin aging process down.

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