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The Effect of Marigold Flowers (*Tagetes Erecta*) Extract on Photoaging: A Literature Review

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A B S T R A C T

Indonesia is a tropical country with high UV exposure. High UV exposure can lead to photoaging as UV radiation accounted to 80% cause of aging. UV A rays have the biggest role in photoaging because they are the most abundant and can reach the deep layers of the skin. Even sunblock cant fully absorb UV radiation. Thus, we need other way to prevent the damaging effect of UV radiation. Antioxidants can play a role in overcoming oxidative stress due to ROS produced by exposure to UV light. One of local ingredient that is rich in antioxidant is marigold flower. Marigold flower has bioactive content of thiophenes, phenols, flavonoids, carotenoids, triterpenoids. Its main component is lutein which is a kind of carotenoid. This literature review used electronic databases on Google Scholar with keywords of "marigold flower (Tagetes erecta) extract, photoaging". Data was collected from national and international published journals. We found four studies about extract treatment in regards of aging caused by UV radiation (photoaging). In conclusion, it shows that marigold flower extract has a great potential as anti-photoaging. Further research is needed to establish the best administration method, and safe effective dosage for anti-photoaging agent.

Keywords: marigold flowers extract, UV, photoaging, antiaging

INTRODUCTION

Indonesia is a tropical country with high sun irradiance throughout the year. For example, a study that was done in Bandung, Indonesia found that the ultraviolet index had reached extreme value (≥10) for 46%.(Hamdi, 2019) High ultraviolet (UV) exposure can lead to photoaging as UV radiation accounted to 80% cause of aging. UV A rays can reach deep into the skin to the dermis layer and increase the risk of skin cancer. Meanwhile UV B rays can only reach the epidermis layer of the skin and cause sunburn, tanning and the formation of carcinogens. UV A rays have the biggest role in photoaging because they are the most abundant and can reach the deep layers of the skin. Even sunblock can't fully absorb UV radiation. For comparison, SPF 100 can only absorb 99% of UV B light exposure.(Bravo & Negbenebor, 2023) Thus, we need other way to prevent the damaging effect of UV radiation. Antioxidants can play a role in overcoming oxidative stress due to ROS produced by exposure to UV light. Antioxidants work to maintain oxygen homeostasis. The mechanism of action is by nucleotide excision repair (NER). DNA damaged by exposure to UV rays is repaired enzymatically and with the help of anti-oxidants. Damaged DNA can be identified, removed and replaced to repair the DNA chain.(Kammeyer & Luiten, 2015) One of local ingredient that is rich in antioxidant is marigold flower. This flower is easily earned and widely used in traditional ceremonies in Bali. Based on previous study, yellow Balinese marigold flower has IC_{50} of 50.641 µg/mL which meant it had a strong antioxidant activity.(Kusmiati et al., 2018) Marigold flower has bioactive content of thiophenes, phenols, flavonoids, carotenoids, triterpenoids. Its main component is lutein which is a kind of carotenoid.(Y. Singh et al., 2020) This review explores the potential of marigold flower extract that is rich in antioxidant as anti photoaging agent. This literature review use electronic databases on Google Scholar with keywords of "marigold flower (*Tagetes erecta*) extract, photoaging". Data was collected from national and international published journals. We sort and used 4 articles for reference.

RESULT

Table 1 - Marigold Flower (*Tagetes erecta*) Extract as Anti-Photoaging

Authors	Study Design	Sample	Intervention	Result
(Maity et al., 2011)	Experimental post test only control group design.	Human dermal fibroblast cell.	Methanol extract of marigold flowers were given to the cell.	Effective inhibition of hyaluronidase, elastase and MMP-1 compared to control group.
(Sachdeva et al., 2011)	Experimental post test only control group design.	120 female Lacca mice.	Topical application of hydroalcoholic extract of marigold flower to the UV irradiated mice.	Application of 2% topical extract treatment reduced malondialdehyde (MDA) level by up to 50 %, increasing glutathione (GSH) level 3-fold ($p < 0.01$), and no signs of histological changes compared to control group.
(Kang et al., 2018)	Experimental post test only control group design.	Human dermal fibroblast cell.	Marigold methanol extract to the UVA irradiated cell.	Increase type 1 procollagen by 83,7%, decrease MMP-2 activity by 36,5%, decrease MMP-1 mRNA expression by 69,5% compared to control.
(Auh & Madhavan, 2021)	Experimental post test only control group design.	48 male Swiss Albino mice.	Mixture of marigold flowers and rosemary extract were given orally to the UV irradiated mice.	Decrease of MMP-1, MMP-3, MMP-10, and MMP-13 expression, decrease of inflammatory mediators, decrease of oxidative stress, and thicker epidermis and dermis compared to control group.

DISCUSSION

Aging is the result of a progressive decline in the physiological function of the body's cells and tissues. In aging, damage accumulates which slowly affects tissue repair capacity. Skin as the body's main barrier is greatly influenced by intrinsic and extrinsic factors (Lyu et al., 2022). Intrinsic factors that can cause the aging process are a decrease in hormones, methylation and glycosylation phenomena, exposure to free radicals, decreased immune system resistance, apoptosis, and the role of genetics. Meanwhile, extrinsic factors of aging are inadequate nutritional intake, unhealthy lifestyle, high levels of stress, and the presence of pollution in the environment (Pangkahila, 2019). The structure of the skin changes during aging, where the epidermis thins by 6.4% per decade. Women's epidermis thins faster than men's. The dermis layer also experiences thinning due to reduced vascularity and cellularity of this layer, especially with the loss of collagen and elastin. The rate of dermis thinning is the same for women and men. In the hypodermis, as we age, the fat pad layer loses(Yusharyahya, 2021).

Signs of aging caused by intrinsic factors include pale, dry skin, reduced skin elasticity, fine wrinkles, and increasingly clear expression lines on the face. This occurs because the epidermis layer thins, the number of mast cells and dermis fibroblasts decreases, collagen production decreases, DEJ / rete ridges become flat. The contact area between the epidermis and dermis is reduced so that the epidermis receives less nutritional supply. Degradation of the extracellular matrix affects skin water retention. Meanwhile, signs of aging caused by main extrinsic factors appear on the face, neck, hands, and to a lesser extent on the forearms and legs. As much as 80% of aging from extrinsic factors is caused by exposure to UV rays (Yusharyahya, 2021).

Photoaging is aging caused by exposure to the sun's UV rays. Most of the 10-400 nm UV rays are blocked by the earth's atmosphere so that the UV rays that reach the earth's surface consist of >95% UV A rays (315-400 nm) and around 5% UV B rays (280-315 nm). Ultraviolet C (UV C) rays (100-280 nm) are completely absorbed by the ozone layer and the earth's atmosphere. UV A rays can reach deep into the skin to the dermis layer and increase the risk of skin cancer. Meanwhile UV B rays can only reach the epidermis layer of the skin and cause sunburn, tanning and the formation of carcinogens. UV A rays have the biggest role in photoaging because they are the most abundant and can reach the deep layers of the skin. Signs appear as rough and deep wrinkles, rough skin texture, fragile skin, purpura, telangiectasis, slow wound healing, pale or yellowish complexion with mottled hyperpigmentation, loose skin, and benign or malignant masses. Microscopically, there is thickening of the epidermis due to failure of corneocyte degradation from desmosomes and impaired differentiation of epidermal keratinocytes. UV rays can also cause abnormal elastin build up, causing elastosis. Microvascular function also decreases because angiogenesis, vasodilation, and expression of adhesion molecules are also disturbed.(Yusharyahya, 2021)

Intrinsically, 1.5-5% of oxygen in the body is converted into superoxide anion radical which is a type of ROS. ROS is a waste product of the electron transport chain in mitochondrial aerobic metabolism. In the skin, the main ROS producers are keratinocytes and fibroblast cells. ROS can form in the first 5 seconds after exposure to UV light based on an in vitro study.(Hofer, 2019) Extrinsically, exposure to UV light can trigger the formation of singlet oxygen. UV A penetrates down to the dermis layer and produces photosensitizer compounds. Excited molecules can transfer energy into heat and emit fluorescent and phosphorescent. The reaction that occurs can be a type 1 reaction where the photosensitizer reacts and produces stable products or free radicals. Type 2 reactions occur when the photosensitizer transfers energy to oxygen molecules, producing singlet oxygen which is a strong ROS oxidant. Photosensitizers that can produce singlet oxygen after exposure to UV A rays are trans-urocanic acid (trans-UCA), riboflavin, tryptophan, and porphyrin. Singlet oxygen produced by exposure to UV A rays damages the side chains of the amino acids tryptophan, histidine, tyrosine, lysine, methionine and

cysteine. Apart from damaging amino acids in structural proteins, oxidation reactions can form other new ROS such as endoperoxidase and hydroperoxidase which can cause protein cross-linking. As a result, the arrangement of structural proteins such as collagen becomes irregular and the protein structure is damaged.(Kammeyer & Luiten, 2015)

Exposure to UV light produces ROS which then activates NF-κB thereby increasing pro-inflammatory cytokines and growth factors such as interleukin-1 (IL-1), tumor necrosis factor (TNF), epidermal growth factor (EGF). Furthermore, the mitogen-activated protein kinase (MAPK) pathway increases and heterodimerization of the transcription factor precursors c-Fos and c-Jun occurs, thus stimulating an increase in AP-1. Increased AP-1 increases the activity of matrix metalloproteinases (MMPs), which are extra cellular matrix (ECM) remodeling endopeptidases that can degrade almost all components of the ECM. MMPs are produced by keratinocytes, mast cells, neutrophils, eosinophils, fibroblasts, and macrophages in the skin. MMPs play an important role in cell repair and tissue remodeling, especially during embryonic development and angiogenesis. The action of MMPs on the ECM is balanced by tissue inhibitors of MMPs (TIMPs). TIMPs regulate ECM turnover, tissue remodeling, and cell activity. Disturbances in the balance of TIMPs and MMPs can have implications for pathophysiological conditions. One of the MMPs activated by AP-1 is MMP-1. AP-1 also inhibits transforming growth factor beta (TGF-β). This has implications for collagen degradation and procollagen inhibition.(Cabral-Pacheco et al., 2020; Poon et al., 2015; Sonoki et al., 2018; Yusharyahya, 2021)

The marigold plant (*Tagetes erecta*) is a plant that originates from the tropical regions of Southeast Asia. There are approximately 53 species of Tagetes worldwide. This plant grows to a height of 50-80 cm with leaves measuring around 5-17 cm. The stems and leaves have fine hairs. Marigold plants grow in Asia, India, China and other countries with tropical climates. A temperature of 20ºC - 30ºC is a good temperature for plant growth. Marigold plants have anti-microbial, insecticidal, hepatoprotective, anti-bacterial, anti-oxidant, larvicidal, wound healing, anti-hyperlipidemic, anti-diabetic, anti-inflammatory, anti-pain effects. Marigold flowers are popular as garden ornamental flowers, used in religious events, the flowers can be consumed as a natural dye extract, and can be processed into essential oil as a perfume ingredient. Marigold flowers can also be used as medicine. The flowers are used as a fever medicine in ayuverdic medicine, astringent, scabies treatment, and eye diseases.(N. Singh, 2019)

Phytopharmaceutical studies on marigold flowers show that the flowers are rich in antioxidants such as thiophenes, phenols, flavonoids, carotenoids, triterpenoids. Marigold flowers contain xantophylls carotenoids (98%) such as lutein (64%), antheraxanthin (31%), α-cryptoxanthin (3%), accompanied by phytofluene, carotenes, zeaxanthin, neoxanthin, violaxanthin, β-carotene , lycopene, phytoene. The active substance and main pigment of marigold flowers is lutein. There are 21,600 – 97,600 µg of lutein per 100 g of fresh marigold flowers. Meanwhile, 4.33 mg of crude lutein was obtained per 10 grams of dried marigold flowers. The lutein content in marigold flower extract is 27.22 ± 1.17 mg/g (Mushtaq & Akram, 2020; Ochoa Becerra et al., 2020; Y. Singh et al., 2020; Susanti et al., 2018; Suwanklang et al., 2023). Other ingredients contained in marigold flowers are β - sitosterol, β- daucosterol, 7-hydroxysitosterol, lupeol, erythrodiol, erythrodiol-3-palmitate, 1-[5-(1-propyn-1-yl)-[2,2-bithiophen]-5-yl]- ethenone, α- terthienyl, quercetagetin, quercetagetin- 7-methyl ether, quercetagetin-7-O-glucoside, kaempferol, syringic acid, gallic acid, 3-β-galalctosyl disyringic acid , 3 α galalctosyl disyringic acid, 6-ethoxy-2,4- dimethylquinoline, oplodiol, (3S,6R,7E)-hydroxy-4,7-megastigmadien-9-one, palmitin, ethylene glycol linoleate, and n-hexadecane (Shetty et al., 2015).

Marigold flower extract has lutein as the highest active ingredient. The antioxidant properties of lutein can help protect the skin from damage caused by free radicals and exposure to UV rays, reducing oxidative stress and damage to collagen which contributes to the skin aging process. Carotenoids bind to cellular retinoic acid-binding protein type I and II receptors in the cytoplasm and retinol-binding protein receptors in the nucleus to inhibit the activation of AP-1 and MMP-1 so that in the epidermis it causes increased proliferation and layer thickness accompanied by a more compact stratum corneum. Meanwhile, in the dermis, glycosaminoglycan synthesis and deposition occurs, accompanied by increased collagen production.(Guan et al., 2021) Research by Kusmiati et al., compared the antioxidant activity of lutein isolates from Cipanas marigold flowers, yellow Bali marigold flowers, and orange marigold flowers. The IC_{50} results were respectively 52.975 µg/mL, 50.641 µg/mL, and 57.574 µg/mL. So it can be concluded that the strongest antioxidant activity is possessed by yellow Bali marigold flowers (Kusmiati et al., 2018). This founding might be caused by lutein content in its flower. Lutein is a yellow pigment which is mostly contained in yellow Balinese marigold flowers.

β-carotene has been shown to guard against damage to mitochondrial DNA caused by UV A rays, as well as mitigate the increase in certain enzymes like MMP-1, MMP-3, and MMP-10 triggered by UV A exposure (Wertz et al., 2004). It also counters singlet oxygen formation from UV A exposure. Phenols and flavonoids play a role in thwarting photoaging by absorbing UV A light, regulating NF-κB, scavenging ROS, and inhibiting MMPs (Torres-Contreras et al., 2022). Phenols, such as catechin and gallic acid, hinder p38 phosphorylation, leading to reduced c-Fos levels post-UV exposure, thus decreasing AP-1 activation and MMP-1 increase.(J. Lee et al., 2021) Catechin and gallic acid have been shown to shield keratinocytes from UV-induced oxidative stress and apoptosis when administered topically (Petruk et al., 2018). Previous studies indicate that flavonoids can curb MMP-9 expression by suppressing the MAPK pathway (H. J. Lee et al., 2018). Additionally, flavonoids inhibit NF-κB and AP-1 pathways, reduce hydroxyl radicals and hydrogen peroxide production, and enhance SOD and catalase expression (Lv et al., 2023).

CONCLUSION

In conclusion, it shows that marigold flowers (*Tagetes erecta*) extract has a great potential as anti-photoaging. It can maintain skin thickness and decrease proinflammatory markers related to photoaging. Further research is needed to establish the best administration method, and safe effective dosage for anti-photoaging.

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