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REVIEW

Bitter melon (*Momordica charantia* L.) antioxidants as an alternative to prevent skin cancer

Gamaliel Twoista Putra, Rinda Dwi Sartika 

Faculty of Military Pharmacy, Defence University of the Republic of Indonesia, Bogor, Indonesia

Keywords

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Correspondence

Rinda Dwi Sartika
Faculty of Military Pharmacy
Defence University of the Republic of
Indonesia
Bogor
Indonesia
rinda.ds7@gmail.com

Abstract

Background: The rise in global average temperature significantly affects human health, particularly through increased sun exposure and ultraviolet radiation. This leads to the formation of Reactive Oxygen Species (ROS), triggering oxidative stress that can damage DNA and potentially cause skin cancer. Endogenous antioxidants like melanin are insufficient to counteract these effects, making exogenous antioxidants crucial for preventing oxidative stress and supporting DNA repair. **Objective:** This review article aims to understand the potential content of antioxidant compounds in bitter melon as a preventive alternative to skin cancer prevention. **Method:** Journal sources related to the keywords "Antioxidant", "IC₅₀", "Skin Cancer", "Phenolic extract" and "*Momordica charantia*" were collected. **Result:** Bitter melon (*Momordica charantia* L.) is one of the plants with high antioxidant content. Bitter melon contains antioxidant compounds such as flavonoids, saponins, beta carotene, vitamin A, vitamin B, vitamin C, etc. Based on the source, bitter melon extract can reach IC₅₀ up to 20,012 ppm, which indicates very strong antioxidant activity. **Conclusion:** Ultraviolet radiation generates free radicals and reactive oxygen species (ROS), leading to oxidative stress that may trigger skin cancer. Antioxidants stabilise free radicals and help prevent this stress. Bitter melon, known for its high antioxidant activity, can serve as a preventive alternative against skin cancer.

Introduction

The year 2023 is expected to be the warmest year on record. According to the European Union's climate office, the Copernicus Climate Change Service (C3S), global temperatures are expected to be 1.48 degrees Celsius higher in 2023 than they were between 1850 and 1900. This rise in temperature will intensify the exposure to UV radiation on Earth.

Sunlight is generally an electromagnetic radiation consisting of three rays with different wavelengths, namely ultraviolet (UV) light, visible light, and infrared light. Ultraviolet light basically functions to activate vitamin D inside the body and treat various diseases (Bahar *et al.*, 2021). However, the greenhouse effect causes sunlight that is exposed to the Earth's atmosphere to be trapped. This causes the ultraviolet rays exposed to the Earth to become excessive. High ultraviolet intensity can have a significant impact on health, particularly on human skin. Effects such as

sunburn, erythema, skin darkening, and premature ageing can lead to long-term consequences, including skin cancer (Adzhani *et al.*, 2022). Based on data from the International Agency for Research on Cancer (IARC), the prevalence of malignant melanoma skin cancer worldwide reaches 331,722 cases, with 65,000 deaths each year. In Indonesia, the prevalence of malignant melanoma skin cancer reaches 1716 cases. Meanwhile, the prevalence of non-melanoma skin cancer in the world reaches 1,234,039 cases. In Indonesia, the prevalence of non-melanoma skin cancer reaches 7,841 cases (IARC, 2022).

Excess sun exposure, along with increased exposure to ultraviolet radiation, which are free radicals, can cause damage to human skin. Exposure to ultraviolet radiation causes the formation of Reactive oxygen species (ROS) and depletion of endogenous antioxidant systems. Oxidative stress occurs when ROS production surpasses the defensive capability of endogenous antioxidants. This will result in DNA oxidation, which

might trigger DNA damage. If the formation of DNA fails to regenerate in the body's regulatory genes, it can lead to carcinogenesis, which is a precursor to skin cancer. Preventive efforts are necessary to counteract the effects of free radicals resulting from excessive ultraviolet radiation exposure. Antioxidants play an essential role in stabilising these free radicals. As we age, the effectiveness of the endogenous antioxidant system in the body decreases in stabilising free radicals. Therefore, exogenous antioxidants, which are not produced by the body but obtained from food sources, play a significant role in reducing ROS generation, preventing oxidative stress, and enhancing DNA repair.

Bitter melon (*Momordica charantia* L.) is a group of *Momordica* plants that are believed to have compounds that are anticancerous and fight free radicals that cause skin cancer. Bitter melon contains flavonoid compounds such as luteolin, camphorol, and quercetin. This plant also contains vitamins A, B, and C, as well as amino acids, calcium, phosphorus, and carotene (Inaku et al., 2023). Phenolic compounds in bitter melon have antioxidant properties that function as sunscreens that absorb ultraviolet rays as protection from exposure to free radicals in sunlight (Nst et al., 2023).

Methods

The research method employed is a qualitative approach based on a literature review analysis. This literature study method involves analysing and summarising previous articles that explain the potential of antioxidants in bitter melon (*Momordica charantia* L.) to prevent skin cancer. The data used in this article are secondary data sources obtained from previous literature. In searching for data sources in journal reviews, an online search for articles was conducted on

the Google Scholar and Crossref databases in July 2024. The keywords used in the search for data sources are antioxidants, IC₅₀, *Momordica charantia*, phenolic extract, and skin cancer. From the search, 294 journals were obtained from Google Scholar and 1,986 journals from Crossref. To avoid using too many articles, criteria are needed to select the relevant articles obtained. The articles searched were journals published during the last five years (2019-2024). The articles specifically discussed the antioxidant potential of bitter melon (*Momordica charantia* L.) as a potential alternative for skin cancer prevention. The method used in the articles is an in vitro approach. The parameter used in the article is IC₅₀.

Results

Table I presents the classification of bitter melon.

Table I: Classification of bitter melon (*Momordica charantia* L.)

Kingdom	<i>Plantae</i>
Division	Magnoliophyta
Subdivision	Magnoliopsida
Class	<i>Dicotyledonae</i>
Order	<i>Cucurbitales</i>
Familia	<i>Cucurbitaceae</i>
Genus	<i>Momordica</i>
Species	<i>Momordica charantia</i> L.

Table II presents an overview of research concerning the antioxidant content in bitter melon.

Table II: Some studies that describe the antioxidant content of bitter melon (*Momordica charantia* L.)

No	Reference	Method	Part of plants	Antioxidant activity	Biological compounds
1.	Situmeang B., 2024	In vitro	Seed	The results of the IC ₅₀ value are 137.99 ppm (moderate category).	Fixed oil, insulin-like protein compounds (vegetable insulin), glycosides (momordin and charantin), alkaloids (momordicine), elasterol, hydroxytryptamine, and folic acid, vitamins (C, A, B1, B12, E), minerals (zinc, potassium, calcium, magnesium, iron, phosphorus, manganese, copper), pantothenic acid, lutein, lycopene and fiber, saponins, flavonoids, and polyphenols (powerful antioxidants), cucurbitan glycosides, momordicin, and caranthin.
2.	Oktafiani G., 2021	In vitro	Fruit	A concentration of 3% exhibits the highest antioxidant activity, demonstrating an IC ₅₀ value of 48.21 µg/mL	Flavonoids, glycosides, saponins, steroids, momordisin, momordin, quarantine, tricosanic acid, resin, resinic acid, hydroxytryptamine, vitamins A, B, and C

No	Reference	Method	Part of plants	Antioxidant activity	Biological compounds
3.	Palanisamy et al., 2024	In vitro	Leaf	The IC ₅₀ value for this extract was determined to be 35 µg/ml. The IC ₅₀ value for this activity was determined to be 89 µg/ml.	Fixed oil, insulin-like protein compounds (vegetable insulin), glycosides (momordin and charantin), alkaloids (momordicine), elasterol, hydroxytryptamine, and folic acid, vitamins (C, A, B1, B12, E), minerals (zinc, potassium, calcium, magnesium, iron, phosphorus, manganese, copper), pantothenic acid, lutein, lycopene and fiber, saponins, flavonoids, and polyphenols (powerful antioxidants), cucurbitan glycosides, momordicin, and caranthin.
4.	Karale et al., 2022	In vitro	Leaf	In contrast, the ethanol extract of <i>Momordica charantia</i> exhibited significant anti-lipase activity, showing an IC ₅₀ value of 27.70±0.15 µg/ml.	Alkaloids, phenolics, saponins, tannins, flavonoids, carbohydrates, amino acids, terpenoids, steroids
5.	Fathonah S., 2019	In vitro	Fruit	Bitter melon fruit has an IC ₅₀ value of 20.012 ppm which indicates its activity is very strong.	Alkaloids, flavonoids, tannins, saponins, triterpenoids

Discussion

Ultraviolet free radicals can cause skin cancer

Sunlight is an electromagnetic wave that is classified into numerous spectra. The wavelengths of infrared light are greater than 760 nm, visible light ranges from 400 to 760 nm, and ultraviolet light is between 200 and 400 nm (Adzhani et al., 2022). The ultraviolet light is then categorised into three distinct classifications. Ultraviolet A (UVA) has a wavelength range of 320 to 400 nm. UV A can develop brown spots on the skin without causing redness. Furthermore, ultraviolet-B light exists with wavelengths ranging from 290 to 320 nm. UVB has a high energy level, which can result in sunburn and premature melanin production. Ultimately, ultraviolet C light has a wavelength ranging from 10 to 290 nm. UV C is the light with the shortest wavelength and maximum energy level among all ultraviolet rays. If the ozone layer is destroyed and UV-C enters the planet, there will be an undesirable effect on human life (Jacob et al., 2020).

Essentially, ultraviolet light is beneficial for humans in the formation of Vitamin D3, in the production of tanning, and in the defence of the body's immune system. However, excessive exposure to ultraviolet light can have a negative impact on humans, particularly in terms of health. Excessive exposure to ultraviolet light can cause sunburn, erythema, and skin darkening, and may lead to skin cancer (Dampati & Veronica, 2020).

UVR exposure is believed to be responsible for skin cancer through two different mechanisms. The first involves the direct mutagenesis of epidermal DNA, resulting in neoplasia. The second correlated to

immune suppression, which allows the growing tumour to elude immune surveillance and grow steadily (Godic et al., 2014).

Ultraviolet radiation can induce the formation of Reactive Oxygen Species (ROS), a type of oxidative stress that leads to increased free radical production. UV light produces a variety of free radicals, including oxygen radicals, singlet oxygen (O₂), hydroxyl radicals (OH), lipid peroxides, and alkoxy radicals. Due to their reactive and unstable nature, free radicals can damage cells. The formation of ROS can also cause gene mutagenesis, such as the transversion of a guanine base to a thymine base, which alters the base pairing of the gene and affects the DNA, thereby promoting abnormal cell growth (D'Orazio et al., 2013).

UVR exposure induces photochemical alterations to genetic material (DNA), although the cell accurately and effectively repairs the majority of the damage. However, if the damage is severe enough, some of the DNA changes may become irreversible mutations. Most DNA breaks are repaired by proteins in the cell nucleus; nevertheless, unrepaired DNA damage can trigger skin cancer (Godic et al., 2014).

Skin cancer is classified into three principal types: Basal Cell Carcinoma (BCC), Squamous Cell Carcinoma (SCC), and Cutaneous Malignant Melanoma (CMM). Basal Cell Carcinoma (BCC) is usually characterised by the appearance of transparent lumps on the face. Although it rarely metastasises, BCC has the potential to become malignant as it can damage and destroy surrounding tissues. This type of cancer seldom causes death and is relatively easy to treat through surgery and radiation therapy. Squamous Cell Carcinoma (SCC) arises in the

squamous cells located within the epidermis. It typically progresses more rapidly than basal cell carcinoma and is often more aggressive, causing significant damage to surrounding tissues. Cutaneous malignant melanoma (CMM), on the other hand, is a malignant tumour originating from melanocyte cells in the epidermis. This type of melanoma is classified into four subtypes: Superficial Spreading Melanoma (SSM), Nodular Melanoma (NM), Lentigo Malignant Melanoma, and Acral Lentiginous Melanoma (ALM) (Tasminatun *et al.*, 2016).

Within the body, key compounds involved in the development and progression of cancer are referred to as oncogenes and tumour suppressor genes. Under normal conditions, oncogenes are responsible for cell growth and division through mechanisms such as chromosome translation, while tumour suppressor genes function to stop excessive cell growth or the development of abnormal cells. However, in cancer cells, the DNA is damaged, resulting in excessive oncogenesis and inactivation of tumour suppressor genes, so the cell growth process becomes uncontrollable. To treat cancer, various therapeutic methods can be employed, including surgery, radiation therapy, chemotherapy, endocrine therapy, and immunotherapy (Adzhani *et al.*, 2022).

Antioxidants can prevent ultraviolet light free radicals

Free radicals are atoms or molecules that contain one or more unpaired electrons, giving them a unique chemical property. The presence of these unpaired electrons results in an uneven distribution of charge, making free radicals either positively or negatively charged and highly reactive. These reactive species play a significant role in various biochemical processes. Free radicals can originate from internal sources (endogenous), where they are formed as byproducts of normal metabolic activities involving proteins, carbohydrates, and fats. Furthermore, they can also be derived from external sources (exogenous), which include exposure to environmental factors such as air pollution, exhaust fumes from vehicles, various industrial chemicals, consumption of charred or carbonised foods, and ultraviolet (UV) radiation from sunlight. These combined sources contribute to the generation of free radicals within the body, which in turn influence cellular function and may lead to oxidative stress (Winarti *et al.*, 2021).

Antioxidants are needed to counteract free radicals, such as ultraviolet rays from sunlight, and stabilise them. The process of stabilising free radicals involves completing the electron deficiency of free radicals to prevent chain reactions. Moreover, antioxidants can

function either as donors of hydrogen radicals or as acceptors of free radicals, thereby helping to delay the onset of free radical formation (Jannah & Widodo, 2014).

ROS can increase the production of free radicals in response to ultraviolet light, enhance the potency of DNA mutations, and promote abnormal cell growth that can trigger skin cancer. Antioxidants help to prevent the production of reactive oxygen species (ROS) through direct breakdown, decrease the concentration of oxidants within and around cells, block ROS from reaching their biological targets, and restrict the propagation of oxidants during lipid peroxidation. (Haerani *et al.*, 2018)

The natural defence mechanisms of our skin, such as melanin and enzymatic antioxidants, alongside the antioxidants we obtain through our diet, like vitamins A, C, E, and others, serve as the primary protection against the harmful effects of ultraviolet (UV) radiation. As a result, dietary antioxidants play a crucial role in maintaining the body's balance of oxidative processes. Key antioxidants found in the human diet include vitamin C (ascorbic acid), vitamin E (α -tocopherol), beta-carotene, and a range of other essential micronutrients, including carotenoids, polyphenols, and selenium. These compounds collectively contribute to safeguarding our cells from oxidative damage. Exposure to UV radiation, however, significantly impacts the skin's antioxidant defence systems. UV radiation induces the formation of reactive oxygen species (ROS), which leads to the depletion of the skin's endogenous antioxidant resources. Some studies have focused on how external (exogenous) antioxidants can influence the protective effects against photoaging and damage caused by UV exposure, highlighting their potential significance for clinical applications and therapeutic practices aimed at reducing the harmful consequences of UV radiation (Godic *et al.*, 2014).

Antioxidants in bitter melon (*Momordica charantia* L.)

Bitter melon (*Momordica charantia* L.) is a fruit vegetable that is a seasonal crop. Bitter melon is less desirable in the community because of its bitter taste. The bitter taste of bitter melon comes from the content of glucoside substances called momorsidin in bitter melon, especially in the fruit and leaves. Though the substance that causes the bitter taste has health benefits (Ritonga, 2019).

Morphologically, bitter melon is a vine with spiral tendrils, many and branched, and ribbed stems. The bitter melon fruit is between 8 and 30 cm long, pointed at the end, green in colour, bitter in taste, and jagged on the surface. Leaves are single, stalked and alternate,

elliptical, 3.5–8.5 cm long, 4 cm wide, 5–7-nerved, with a heart-shaped base, and dark green in colour. Flowers are single flowers, androgynous in one tree, long-stemmed, and the crown is yellow (Ritonga, 2019).

Bitter melon plants contain compounds that are antioxidants, such as flavonoids, quercetin, saponin, vitamins A, B, C, beta carotene, etc. These compounds function as antidotes to free radicals, such as ultraviolet radiation from sunlight, that causes damage to the skin. Here are some journals that record the antioxidant content of the bitter melon plant.

From the data collected, it was noted that bitter melon exhibits high antioxidant activity. IC₅₀ (inhibition concentration) is the concentration of the sample solution needed to inhibit 50% of DPPH free radicals. The smaller the IC₅₀ value, the stronger the antioxidant is in counteracting free radicals or can be said to have more potent antioxidant activity. A substance or compound is said to have a powerful antioxidant activity value if the IC₅₀ is less than 50 ppm, a potent antioxidant if the IC₅₀ value is between 50-100 ppm, a moderate antioxidant if the IC₅₀ value is 100-250 ppm, a weak antioxidant if the IC₅₀ value is 250-500 ppm, and an inactive antioxidant if the IC₅₀ value is > 500 ppm (Budaraga & Putra, 2021).

In the antioxidant test, bitter melon has an IC₅₀ value below 50 ppm, which indicates its activity is robust. The IC₅₀ value of bitter melon can reach 20.012 ppm. The IC₅₀ value below 50 indicates that bitter melon has potent antioxidant activity. The compounds contained in bitter melon that are antioxidants are flavonoids, vitamin A, vitamin B, quercetin, saponins, beta carotene, etc. Flavonoids are a group of phenol compounds that have aromatic rings connected by three carbon bridge atoms. Flavonoids have three ways of working as antioxidants to counteract free radicals. The first mechanism involves reducing the formation of ROS by activating endogenous enzyme signals, thereby preventing the production of hydrogen peroxide (H₂O₂) and the hydroxyl radical (OH). The second mechanism involves destroying the ROS. The last mechanism consists of regulating and protecting against free radicals as antioxidants by donating hydrogen atoms (Alfaridz & Amalia, 2018). Beta-carotene is an antioxidant that can help prevent cancer cells by stimulating the immune system (Handayani et al., 2022). The level of content of antioxidant compounds in bitter melon will affect the antioxidant capacity of bitter melon. The higher the content of antioxidant compounds, the greater the antioxidant activity.

Conclusion

Sunlight produces free radicals from ultraviolet radiation that can have a negative impact on human health, particularly damaging the skin and even causing skin cancer. Antioxidants play an important role in counteracting these free radicals through stabilising free radicals that have odd electrons. Antioxidants become contributors to hydrogen radicals or free radical acceptors. Bitter melon (*Momordica charantia* L.) has moderate to potent antioxidant activity. Bitter melon can reach the IC₅₀ value of 20.012 ppm, which means it has potent antioxidant activity, especially in the fruit part.

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