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Review of Phytochemical and Pharmacological Effects of Apple

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ABSTRACT

Apples are the edible fruit produced by the apple tree *Malus domestica*. The apple tree is cultivated worldwide and is the most widely grown species in the genus *Malus*. The apple tree originates from Central Asia. Apple has been developed for thousands of years in Asia and Europe and brought to North America by European colonizers. Apple has a high nutritional value so that it can be a good food source. Humans widely consume an apple. Different cultivars are bred for a variety of flavors and uses, including cooking, eating raw, and juice production. Phytochemically, apples are reported to contain triterpenoids, flavonoids, organic acids, and sterols. Pharmacologically, this fruit is reported to have Antioxidants, Antiobesity, Anticholesterol, Anticancer, Enzyme Inhibitor and Antimicrobial.

Keyword: *Apple, Phytochemical, and Pharmacological*

INTRODUCTION

The scientific name for the apple tree in Latin is *Malus domestica*. Apples grown from Malus sieversii are descendants of Central Asia, with most of the genome of Malus sylvestris. Apples are usually red when ripe and ready to eat, but also can be green or yellow skin, fruit skin a bit soft, the meat was hard. This fruit has several seeds in it. The first began to grow apples in Central Asia. Apple today grown in many regions of the world where the air temperature is cooler. Most apples eaten raw or cooked and are also used in many food pasta. Apples are cooked until they become mushy for applesauce. Apples are also made into apple cider drinks. [1]

Figure 1: Fruit of Apple. [2]

Figure 2: Flowers of Apple. [2]

Scientific classification [1]

Kingdom	: Plantae
Division	: Magnoliophyta
Class	: Magnoliopsida
Order	: Rosales
Family	: Rosaceae
Subfamily	: Maloideae or Spiraeoideae
Nation	: Maleae

Genus : Malus
Species : *M. Domestica*

Binomial name:
Malus domestica

Synonym Apple [1]

- *Malus communis Desf.*
- *Malus pumila* Mil.
- *M. frutescens Medik.*
- *M. paradisiaca* (L.) Medikus
- *M. sylvestris* Mil.
- *Pyrus malus L.*
- *Pyrus malus var. paradisiaca L.*
- *Pyrus dioica Moench*

DATA COLLECTION

In compiling this review article, the technique used is by searching for sources or literature in the form of international journals in the last 20 years (2000-2020). The primary references in this article are through websites such as ScienceDirect, Pubmed, Google Scholar, Pubchen, and other trusted journals with the keyword as follows: apple, *Malus domestica*, phytochemicals, and pharmacology.

PHYTOCHEMICAL REVIEW

The phytochemical properties of apples were determined by using the chromatographic analysis method showed that the triterpenic content was 9,586 mg/g of pomace. Ursolic acid comprises 7,125 mg/g (about 75% of the total). The amount of triterpenic acid synthesis was also obtained as much as (0.287 mg/g in pomace. And the total content of sterols and their derivatives in pomace was 1.716 mg/g. [19]
The results obtained, the total phenol content of apples is 31.5-980.8 GAE/g. Flavanol content in apples is 0.004-0.185 QEA (mg/g), flavonoids range from 0.36 to 0.3584 QEA (mg / g). The maximum phenol 980.8 GAE/g, this study uses Mallus apple floribunda wild type, followed by 722.0 GAE/g on Early Tydemans Worcestor and minimum phenolic content of 31.5 mg L 1 was observed in Starking Delicious. Other types have a moderate range. QEA maximum flavonoid content is 0.3884 (mg/g) was observed in the wild apple floribunda types Mallus followed by Ambri (0.367 QEA (mg/g), and a minimum of 0.024 QEA flavonoid content (mg/g) was observed in Star Summer Gold, followed by QEA 0.027 (mg/g) in apples rich in another type has a moderate concentration Additionally, maximum (0.351 QEA (mg/g) and minimum (0.002 QEA (mg/g) flavanol content) was observed in Val Orange and Red Fuji. [16]

Determination of chemical constituents of skin Red Delicious apples bioactivity using the method of fractionation. Some of the compounds, including triterpenoids, flavonoids, organic acids, and sterols were isolated using a solvent gradient fractionation, ODS Diaion HP-20, silica gel, and column, and preparative HPLC. Based on the results of the isolation of flavonoids, the main flavonoids in the skin of apples are quercetin - 3 - O - D - glucopyranoside (82.6%), and quercetin-3-O - D-galactopyranoside (17.1%), quercetin (0.2 %), (-) -catechin, (-) - epicatechin, and quercetin - 3 - ORL - arabinofuranoside. [8]

Phenol content of varieties Gala, Fuji and Golden Delicious that 95% is produced by Brazil. Phenols (whole fruit) were determined by HPLC, total phenols determined using the Folin-Ciocalteau. Golden Delicious has the highest phenol content (408 mg/fruit) than Fuji (194 mg/fruit) and Gala (162 mg/fruit), three varieties phenolic profile shows 5-caffeoylquinic acid, (2)-epicatechin, procyanidin B2, and phloridzin as a main component with procyanidins as the main class and quercetin as a minority. The results showed that the phenol content of the varieties Gala, Fuji and Golden Delicious that 95% is produced by Brazil.Phenol (whole fruit) were determined by HPLC, the amount determined by the method of Folin phenol-Ciocalteau. Golden Delicious has the highest content of phenol (408 mg/fruit) compared to Fuji (194 mg/fruit) and Gala (162 mg/fruit), phenolic profile of the three varieties showed 5-caffeoylquinic acid, (2)-epicatechin, procyanidin B2 and phloridzin

as a main component with procyanidins as the main class and quercetin as a minority. [21]

From phytochemical studies, it was found that the total phenolic levels (TPC) were tested by the Folin-Ciocalteu method, HPLC/DAD determined individual phenolics, and TAC was measured using iron-reducing antioxidant power (FRAP). Ten grams (10 g) of skin and fresh frozen meat were taken per apple genotype. Then dilute methanol in a ratio of 1: 1 (w/v), the mixture is filtered, the filtrate is stored at 20 ^{o}C before analysis. The results showed that procyanidin was the most dominant phenolic group in meat and skin, followed by hydroxynamic acid in flesh and flavonol in the skin. [10]

PHARMACOLOGICAL ACTIVITY

Antioxidant

Apples are carcinogenesis using a test system in-vitro and in-vivo. Apple phytochemical content such as flavonoids (catechins, flavonols, quercetin) and phenolic acids (glycosides of quercetin, catechin, epicatechins, procyanidins), vitamins, and fiber, which provides the benefits of antioxidants. The use of natural materials or synthetic is to prevent and inhibit the development of carcinogenesis and can reduce the risk of invasive clinical disease. [13]

The results showed that AgNP can be the best alternative to antibiotics for the infection control triggered by the MDR strain of bacteria. [21] In this study, the agar diffusion test is used to describe M.domestica-AgNPs antibacterial activity against clinical isolates of drug resistance in the test. After 24 hours of incubation, clear zones of inhibition observed in the well is filled with AgNPs M.domestica- and ciprofloxacin/chloramphenicol (positive control). It was found that M.domestica-AgNPs have the highest activity against Enterobacter aerogenes, (24mmat 500 ug/mL), Klebsiella pneumoniae (23mmat 500 ug/mL), Pseudomonas Aeruginosa (22mmat 500 mg/mL) and Escherichia coli (8mmat 500 mg/mL). The results showed that the MIC of M.domestica-AgNPs found to be 35.59 ug/mL for Enterobacter aerogenes, 34.17 ug/mL for Escherichia coli, 27.47 ug/ml for Pseudomonas Aerogenosa, and 24.56 mg for Klebsiella Pneumonia. The findings clearly show that it is stable AgNPs have excellent antimicrobial activity against MDR strains of *Enterobacter aerogenes* and the results further indicated that the antibacterial activity of *M.domestica*-AgNPs were equal to the antibacterial activity of 20 µg positive control antibiotics. [3]

From the results of studies, that consumption of apples has been proven effective for relieving symptoms of intestinal inflammation. This effect is because apples contain (poly) phenols, including phloretin (Phlor) and glycosides called phloridzin (Phldz).The modulation effect of these molecules can be seen from their impact on synthesisproinflammatory molecules (PGE2, IL-8, IL-6, MCP-1, and ICAM-1) in IL-1-treated myofibroblasts of the colon CCD-18Co cell line) the potential for further inhibition of glycation formation final products (AGEs). The results showed that Phlor (10–50 M) decreased the synthesis of PGE2and IL-8 and the formation of AGEs by different mechanisms. [23]

Antiobesity

The results of research conducted on adult male Wistar rats gave an inhibitory effect of supplementation with apple pectin molecule on obesity. The phytochemical effects of apple viz pectin against the oxidative effects of a high-fat diet observed. The study results stated TBARS concentration in the liver, kidney, and blood serum of mice that received a high-fat diet, and simultaneously apple pectin (HFD + Pec) decreased by 20%, 29%, and 19%.Tests carried out in this study were carried out on a total of 28 adult male Wistar rats weighing 230 10 g. [15]

Thin young apple polysaccharide (TYAP) has been investigated in a high-fat

diet (HFD) induced fat rat due to its effect on metabolic disorders. Administration of TYAP at doses of 400 mg/kg/day and 800 mg/kg/day significantly saved HFD induced hepatic metabolic disorders, reduced weight gain, and improved liver oxidative stress caused by HFD. The results of this study suggest that TYAP is successful in lowering obesity-related hepatic metabolic disorders, possibly by activating hepatic mitochondrial respiratory function. [5]

This study is to encourage women's weight loss at a rate of 1 kg/month. After 12 weeks of weight loss, results obtained 1.21 kg. A decrease in blood glucose was also observed for women who consumed fruit (5.2 mg / dL, P 0.02). [12]

Anticholesterol

ACT research shows the interaction between the cholesterol (CH) enables new hypocholesterolemic mechanism apple condensed tannin (ACT). The results showed that the quenching of fluorescence by CH ACT conducted in accordance with the static mechanism. Conversely, interaction between ACT and CH in vitro is a spontaneous process. ACT is able to bind with direct CH, and CH-binding capacity (35.9 to 43.9%) of the ACT are greatly enhanced with increased concentration of ACT (proanthocyanidin B2 0.5 to 2.0 mg equivalent/mL).Spectroscopic and analytical methods used to characterize the morphology of coprecipitates ACT-CH, the results showed that the ACT is able to precipitate CH via ionic interactions, hydrophobic interactions and hydrogen bonding rather than covalent intermolecular. In conclusion, the direct exchange with CH ACT may play a role in their CH-lowering effect in humans and animals. [22]

Apple peels can inhibit the oxidation of lipoprotein cholesterol (LDL-C) because apple skin contains quercetin and triterpenes, the constituent compounds, and three metabolites of quercetin in vivo. The results of this study showed that the IC50 value of the quercetin for LDL-C oxidation products was 0.06–8.29 mg / L and the TAE for LDL-C oxidation products was 29.58–95.49 mg / L. Overall, both extracts effectively inhibited LDL-C oxidation in vitro. [17]

Analysis of the chemical composition of Gala apples studied to determine the effect of serum total cholesterol, HDL-C, LDL-C, triglycerides, cholesterol liver, and feces. for treatment used as many as six animals. this study observed control apples, 5, 15, and 25% for 30 and 60 days. derived phenolic compound (0.38 g, 100 g^{-1}) and tannins (0.16 g-100 g^{-1}), the reduction in apples 15% and 25% showed a significant reduction of LDL-C and cholesterol levels and increase if compared to control. Apples 25% reduction provides a significant reduction in hepatic cholesterol levels compared with the control group. [14]

Based on the study results, that apple fiber and polyphenols can play a role in preventing atherosclerosis by lowering plasma uric acid. Uric acid was determined in plasma using a commercial kit, plasma total cholesterol, and triacylglycerol (TAG) were tested using an enzymatic assay. [4]

Anticancer

The study was conducted to assess the likely effect of the resilience of apple polyphenols, with particular attention to the carcinogenic anthocyanin colon, slowing or reducing the appearance of various markers of precancerous. Colorectal cancer (CRC) is the fourth cancer with the most recent cases reported in 2018 worldwide. Besides apples contain flavonoids, also contain anthocyanins, especially sianidin-3-O-galactoside (Cy3Gal). Research shows that mice that were fed apples WF and RF showed the incidence of ACF lowest in ST (8 weeks after injection of AOM).In contrast, the LT (14 weeks after AOM injection), only food supplementation with apple WF capable of reaching the ACF inhibition of 41.3%, due to higher daily intake of flavan-3-ols / flavonols, which alter gene expression associated. With the apoptosis associated with ACF and MDF, a known marker of precancerous colorectal

carcinogenic. From all the data mentioned above, our research shows the effects of apple polyphenols and Cy3Gal on carcinogenic colon, slowing or reducing the appearance of various markers of precancerous studied. [6]

Total phenolic flavonoids from *Red delicious* (RD) are 8.03 ± 0.05 b, Fuji (FJ) is 5.92 ± 0.05 d, *Golden delicious* (GD) is 6.97 ± 0.05 c, and *Granny smith* (GS) is 8.73 ± 0.04 a. For the IC50 value of apples, RD is 1.38 c (1.23–1.54), FJ apples are 2.62 A (2.42–2.81), GD apples are 1.87 b (1.73–2.01), GS apples are 1.12 d (1.01–1.21). The index value obtained for GS apples is 0.95, RD apples are 0.86, GD apples are 0.67, FJ apples are 0.55. Of all the apple cultivars evaluated to inhibit cell growth, apple cultivars differ significantly from each other in the extract concentration required to inhibit cell growth by up to 50%. From the results of the study, it was concluded GS was the most effective cultivar to inhibit cell growth, followed by apple RD, GD, and FJ extracts ($P < 0.0001$). [18]

Studies show the results of bioactivity against cancer cells. Triterpenoids antiproliferative activity against human HepG2 liver cancer cells, breast cancer cells MCF-7 and colon cancer cells Caco-2 were evaluated. Triterpenoids activity seems high against three human cancer cell lines. 2α-hidroksiursolat acid, 2α-hydroxy-3SS - {[(2E) -3-phenyl-1-oxo-2-propenyl] oxy} olean-12-en-28-OIC acid and trans-p-3SS acid Coumaroyloxy-2α-hydroxyolean-12-en-28-OIC showed antiproliferative activity higher than HepG2 cancer cells.Ursolic acid, 2α-hidroksiursolat acid, and the acid-trans- 3SS p-coumaroyloxy-2R-hydroxyolean-12-en-28-OIC indicates a higher antiproliferative activity against cancer cells MCF-7. The results of the test triterpenoids show antiproliferative activity against Caco-2 cancer cells, especially acid-hydroxyursolic 2α, maslinic acid, 2α-hydroxy-3SS - {[(2E) -3-phenyl-1-oxo-2- propenyl] oxy} olean-12-en-28-OIC acid, and 3SS-trans-p-coumaroyloxy-2R-hydroxyolean-12-en-28-OIC acid, which shows the antiproliferative activity much higher. Triterpenoids isolated from the skin of apples have potent anti-proliferative activity and can be used as anticancer. [9]

The research study proved that the phytochemical content of selected apple extract on TNF-induced NF-κB activation in human breast cancer MCF-7 cells at a dose of 5 mg / mL ($p < 0.05$) significantly blocked the NF-κB-induced activation. TNF-R from MCF-7 cells. Phytochemical cytotoxicity measurements and selected apple extracts used methylene blue assay, and the cells were stored at 37 ° C in 5% CO_2 for 24 hours. The methylene blue staining was eluted with an elution solution consisting of 49% (v / v) PBS, 50% (v / v) ethanol, and 1% (v / v) acetic acid. Furthermore, the absorbance was measured at 570 nm by the MRX II Dynex plate reader. [20]

Inhibition Enzyme

The presence of triterpene acids, such as betulinic acid, oleanolic acid, ursolic acid, maslinic acid, erythrodiol, and uvaol in apples, of which ursolic acid and oleanolic acid are the most abundant in apples known by using the HPLC-MS analysis method. Triterpenic acids, such as uric acid, betulinic acid, and maslinic acid, exhibit strong antioxidant and enzyme inhibitory effects. Ursolic acid exhibits a competitive inhibition type for tyrosinase, IC50 values are 13.2-30.8 μg / mL (tyrosinase), 19.6–42.5 μg / mL. For research results from apple methanol extract and three triterpenic acids (TTA), namely, Ursolic acid, maslinic acid, and oleanolic acid exhibited strong anti-cancer effects against Hela, Skov-3, Caski, and NCL cancer cell lines. Ursolic acid exhibits competitive inhibition type for tyrosinase, Ursolic acid (IC50 of 6.5 ± 0.7, 15.5 ± 1.4, 20.8 ± 1.3, and 5.6 ± 0.8 μg / mL). The anticancer activity was prominent on Hela, Skov-3, Caski, and NCL cancer cells. [11]

Antimicrobial

The total polyphenol content and partial phenolic composition of the pulp and skin were produced organically and conventionally *Malus domestica*. Organically grown apples show a higher content of polyphenols, both in the pulp and skin. The results of the study, the use of Annurca apple peel extract grown organically, has antimicrobial activity against several food-borne bacteria such as entemorragic. *E. coli*. Meanwhile, conventionally produced apples showed good inhibitory effects against *Bacillus Cereus*. [7]

CONCLUSION

Apples have a lot of phytochemical content, namely, by using the chromatographic analysis method, the triterpic results were 9,586 mg/g of pomace. Ursolic acid 7,125 mg/g (about 75% of total). The synthesis of triterpenic acid was also obtained as much as (0.287 mg / g in pomace. And the total sterol content is 1.716 mg / g. The total phenolic content in apple ranges from 31.5 to 980.8 GAE / g. Flavanol content is 0.004 to 0.185 QEA. (mg / g), flavonoids ranging from 0.36 to 0.3584 QEA (mg / g), the bioactivity fractionation method on Red Delicious apple skin is used to determine the chemical content in apple skin is quercetin - 3 - O - D - glucopyranoside (82.6%), then quercetin-3-O - D-galactopyranoside (17.1%), from quercetin (0.2%), (-) -catechin, (-) - epicatechin, and quercetin - 3 - ORL - Arabinofuranoside. Apples also have a pharmacological effect as an antioxidant, anti-obesity, anti-cholesterol, anti-cancer, enzyme inhibition, and anti-microbial.

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