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Review Article
Phytochemical and Pharmacological Aspects of Anthocyanins

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Abstract
Anthocyanin is a natural compound in plants which comes under the phenolic compounds class. It is responsible for imparting attractive colors in the plants like red, purple and blue. Since, ancient times, plants containing anthocyanins have been used in herbal remedies to treat different medical conditions. The aim of this review article was to provide comprehensive information about the chemistry, stability, pH influences and different pharmacological activities exhibited by anthocyanins and emphasis its importance. Anthocyanins are known to possess antioxidant, anti-inflammatory, anti-cancer, anti-diabetic, cardiovascular and neuroprotective activity. It was also reported that anthocyanins contribute in enhancing learning and memory. In industrial field, anthocyanins are used as natural food colorants and this is for their relative safety when compared to the synthetic food colorants.

Key words: Anthocyanin, antioxidant, pigment, pharmacological activity, natural colorants, phenolic compounds, phytochemical

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INTRODUCTION

Phenolic compounds are vital constituents that are abundant in a wide variety of fruits and vegetables and they have a role in their sensory properties like bitterness and astringency[1]. As described in Holy Quran, "The fruits like olive, grape, date, fig and pomegranate are gifts and heavenly fruits of God", these fruits contain large amounts of phenolic compounds like anthocyanins, flavonoids, coumarins and tannins[2]. Anthocyanins are classified as phenolic compounds and they are water-soluble pigments[3].

The origin of the word anthocyanin comes from a Greek word that was used to describe a pigment which is blue, that cornflower (*Centaurea cyanus)* contained[4]. They are responsible for most of the bright and shiny colors as blue, pink, purple, red and orange that can be seen in most of the fruits, leaves, flowers and cereal grains[5].

The type and quantity of anthocyanins range extensively among diverse plants species. This result in a variation of anthocyanin intake levels widely by season, region and individuals factors like culture and education[6].

ANTHOCYANINS CHEMISTRY

Anthocyanins are considered as flavonoids, but due to their ability to form flavylium cation (Fig. 1) they can be easily identified or distinguished from the rest of flavonoids compounds[7]. They can be classified into two types, glycosides and acyl glycosides based on their aglycone anthocyanidins (Fig. 2)[8]. In a fresh plant, it is rare to find aglycones. Seventeen anthocyanidins can be found in nature, but only cyanidin, petunidin, pelargonidin, delphinidin, malvidin and peonidin are widely distributed and available (Fig. 3)[9]. Anthocyanins vary in the position and number of methoxyl and hydroxyl groups on the primary anthocyanidin structure[10]. This means that the anthocyanin component is identified

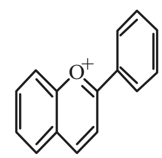

Fig. 1: Flavylium cations structure
Source: Miguel[7]

Anthocyanidin	R1	R2
Pelargonidin	H	H
Cyanidin	OH	H
Peonidin	OCH_3	H
Delphinidin	OH	OH
Malvidin	OCH_3	OCH_3
Petunidin	OCH_3	OH
R_3	OH, glycosyl	
R_4	OH, glycosyl	

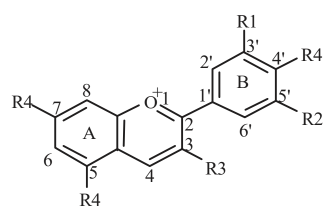

Fig. 2: Structure of anthocyanidin
Source: Ghosh[8]

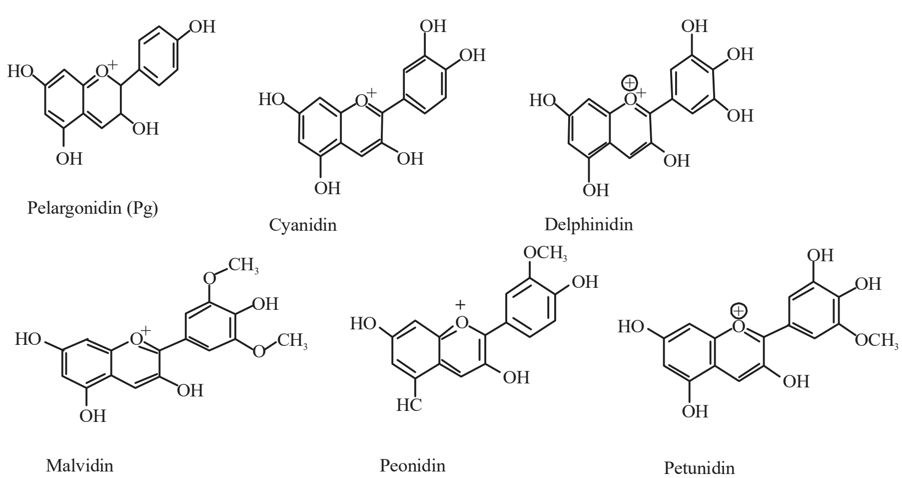

Fig. 3: Structure of naturally occurring anthocyanidins
Source: Pervaiz *et al.*[9]

based on the number and position of the sugar linked. In addition, it is determined by the acylating agent identity and sugar acylation identity.

Anthocyanin occurs mainly as glycosylated anthocyanidin which means that one or more sugar or acylated sugar is attached to aglycone. There are four common substituted mono-sides: Arabinose, rhamnose, glucose and galactose[11]. The glycosylation process provides stability to anthocyanins and anthocyanidins are found to be less stable. Basically, anthocyanins structure has 2 parts: Chromophore (a light-absorbent) which will be called anthocyanidin with a glycoside attachment. Cyanidin-3-glucoside is one of the common anthocyanin structure found in plants[12]. The chromophore which is basic in anthocyanins is a 7-hydroxy flavylium ion. Anthocyanins that occur naturally mainly have hydroxyl substituents at positions 3 (Permanently glycosylated, adding thermal stability) and 5 (occasionally glycosylated) and one or additional methoxy or hydroxy substituents is contained in the 2-phenyl or B-ring[13].

STABILITY OF ANTHOCYANINS

Anthocyanins stability is influenced by many factors like changes in pH, oxygen existence, the chemical composition of the whole structure, applying UV-radiation chemical interactions with consumed food causing metal ions chelation and changes in temperature and light[14]. The influence of these factors results in changes and degradation of the colors. However, some studies showed that if other synergistic antioxidant constituents present, it may contribute to the inhibition or decreasing of anthocyanin degradation[15].

In a study conducted to evaluate the temperature influence on the degradation of anthocyanins, it was found that temperature has a significant effect on the anthocyanin pigment stability whether light is present or absent[16]. In a study performed on anthocyanins present in sorghum plant, it was found that the methanol which was acidified first and used for the extraction had a higher stability than the methanol extract without the acidification process and the discoloration by 2 ways of extraction was directly proportional with the increase in temperature, time and light[17].

The change of color of plants containing anthocyanins sometimes occurs due to enzymatic degradation or browning. This occurs due to the oxidation of phenolic compounds as they convert to o-quinones enzymatically. There are 2 enzymes responsible for this process, polyphenol oxidase (PPO) and peroxidase (POD), because of the structure of anthocyanin which contains a sugar moiety, the PPO enzyme has low affinity against anthocyanin as a result of steric hindrance. If phenols are present the activity of PPO against anthocyanins increases due to increased oxygen consumptions. The PPO can be found in plum, strawberry, grape and blueberry[18,19].

pH INFLUENCE

Basically, anthocyanins color intensity is greater in acidic condition. The change in anthocyanins color is more in alkaline conditions due to instability and degradation. The explanation for this behavior is possibly due to the interaction of the red flavylium cation with co-pigments present which will result in changing the adsorption properties of the solution containing anthocyanins and this at the end will create a more stable anthocyanin extract and protect the color features of the particular solution[20].

At different pH conditions, the structure of anthocyanin differs. In a solution of pH = 1, the red color predominates as flavylium cation. When the pH increases, a competition which is thermodynamic and kinetic starts between the proton transfer reaction associated with the acidic hydroxyl groups of the aglycone and the hydration reaction related to the flavylium cation. In a range of pH = 2-4, blue color predominate as a quinoidal species. At pH values range from 5-6, carbinol pseudo base and chalcone species which are colorless present. When the pH values are greater than 7 degradation of anthocyanins occurs which depends on the substituent groups. Depending on the pH in a range of 4-6 anthocyanins can be identified in different 4 forms which are flavylium cation, carbinol without any color, quinoidal base which is anhydrous and a chalcone with a light yellow color[21].

PHARMACOLOGICAL ACTIVITIES REPORTED OF ANTHOCYANINS

Anti-oxidant activity: It was observed in studies that anthocyanins contribute to protecting cells by preventing cells and tissue damage caused by oxidant stress. Consumption of foods reach in anthocyanin could contribute to modulating specific secondary physiological changes of the oxidant stress and thus preventing obesity[22]. Phenolic compounds like anthocyanins extensively distributed in plants which have been reported to exert different pharmacological effect, including antioxidant activity[23]. The 1,1-diphenyl-2-picrylhydrazyl (DPPH) mostly used for the estimation of free radical-scavenging activity of plant antioxidants[24].

Anti-inflammatory activity: In a study that was conducted to analyze the anti-inflammatory properties identified in anthocyanins, it was proved that cyanidin-3-glucoside metabolites were effective under physiological conditions as anti-inflammatory agents for the endothelial cells in the vascular system of humans[25].

Anti-cancer activity: Secondary metabolites are major sources of new chemical compounds for development of new medicines including anticancer agents[26].

The fast growth in the cancer problem denotes a crisis for healthcare systems around world and there is need for search of better drug control cancer[27].

Due to anti-oxidant, anti-mutagenesis and anti-inflammation properties it was found that anthocyanins have the ability to inhibit propagation of cells by modifying the pathways of signal transduction, which will result in stimulating cell cycle arrest and inducing apoptosis or in other term autophagy of tumor cells. It was observed that anthocyanins have the ability to increase the tumor cells sensitivity to chemotherapy drugs and thereby reversing and reducing drug resistance[28].

Cardiovascular effect: It was found that the consumption of anthocyanins contributes to the treatment of chronic diseases such as; Cardiovascular Diseases (CVD). This is due to the chemical structure of anthocyanin, preventing endothelial dysfunction and inflammatory processes[29].

Antidiabetic activity: Many studies supported that anthocyanins prevent the occurrence of diabetes mellitus[30]. It was found that anthocyanins by the up regulation of insulin-regulated glucose transporter (GLUT4), it controlled the carbohydrate metabolism and that peroxisome proliferator-activated receptor-γ (PPARγ) found in skeletal muscles and adipose tissue was activated by anthocyanins[31]. Anthocyanins works on α-glucosidase along with pancreatic α-amylase to metabolize, digest carbohydrates and thus, decrease the glucose level in the blood and this mechanism mimics to some extent the way acarbose works on our body. Along with that, it was also found that anthocyanins improve insulin resistance, raise insulin sensitivity and uptake of glucose[32].

Neuroprotective activity: Anthocyanins properties such as; anti-neuroinflammatory, anti-apoptotic and antioxidant have a therapeutic effect in the treatment of neurodegenerative diseases such as; Parkinson's disease[33].

Learning and memory enhancing effects: In a study conducted to evaluate the effects of anthocyanins in learning and memory, it was found that it decreased the level of lipid peroxidation damage in the brain which will slow down memory damage that result from oxidative stress. Overall, it was found that anthocyanins provide an improvement in learning and memory[34].

MEDICINAL USES

From many years ago, anthocyanin was contained in the human diet and was used traditionally in form of herbals owing to their physiological ability to treat many conditions such as; liver disorders, hypertension, diarrhea and dysentery, pyrexia, common cold and urinary problems[35].

For instance, *Hibiscus* sp. which contains anthocyanins have been used in folk medicines in the past to treat hypertension and liver dysfunction. Anthocyanins found in bilberry (*Vaccinium*) were historically used as a traditional remedy for diarrhea, microbial infections and vision disorders[36].

INDUSTRIAL USES

To improve the appearance of foods, industries use synthetic colorants. However, synthetic colorants caused considerable side effects and natural colorants extracted from anthocyanins proved they have more benefits with almost absence of adverse effects[37,38]. Anthocyanins provide a wide range of intensive pigments such as; orange, purple, blue and red colors. Examples of plants reach with anthocyanins pigments are red grapes, blueberries, purple corn, strawberry, elderberries, black chokeberries, black currants, cranberry and radish potato[39]. Extraction of the natural pigments is usually done by homogenization and then solvent extraction. In industries ethanol is preferred for the extraction because methanol is associated with toxicity[40].

CONCLUSION

Anthocyanins in many food and drinks appear to have an important role in the prevention of diverse diseases. In the last few years, synthetic food dyes have been banned in many countries because of their poisoning and carcinogenicity. Anthocyanin are coloured natural compounds that are easily obtained from fruits and vegetables can be considered as a possible alternative to banned food dyes. In fact, have shining attractive colors, while its high solubility allows for easy integration into aquatic diets. The nutrient-rich extracts are increasingly attractive to the food industry as natural substitutes for the synthetic dye.

SIGNIFICANCE STATEMENT

This review discovers the phytochemicals and pharmacological activities of anthocyanins that can be beneficial for healthcare management. This study will help the researcher to uncover the critical areas of pharmacological activities of anthocyanins that many researchers were not able to explore.

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