Impact Of Polyphenols On Cholesterol Esterase Inhibition – A Mini Review

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Abstract - Cholesterol, one of the most essential components of cell membrane plays a vital role in the function of cell membrane fluidity, synthesis of sex hormones, bile acid and salt, and is synthesized in adequate amount by the liver. But, increased level of dietary cholesterol may increase the blood cholesterol level, a precursor for the cause of hypercholesterolemia. Therefore, an increase in the serum cholesterol level can cause hypercholesterolemia and prolonged condition leads to the occurrence of various types of cardiovascular diseases. There are various mechanisms to prevent hypercholesterolemia and one such strategy is the inhibition of cholesterol esterase (CEase), an enzyme that hydrolyzes the cholesterol ester to free fatty acid and cholesterol. The inhibition of cholesterol esterase prevents diseases such as hypercholesterolemia, dyslipidemia and related diseases such as atherosclerosis, cardiac arrest, stroke and heart attack. Recent approach is the recruitment of plant based polyphenolics for the inhibition of cholesterol esterase and thereby, the prevention of the above cited diseases can be inhibited by polyphenols from plant sources.

Key Words: Cholesterol esterase, Polyphenols, Hypercholesterolemia, Cardiovascular disease.

1. INTRODUCTION

Cholesterol is one of the most essential components of cell membrane and is derived from the dietary sources and also synthesized endogenously in liver. Cholesterol esterase is the major enzyme responsible for the hydrolysis of dietary cholesteryl esters to free cholesterol that are absorbed by the body. Hence, various mechanisms have been explored to inhibit the cholesterol esterase in order to prevent the entry of dietary cholesterol into the blood and thereby, maintenance of normal homeostasis. One such novel approach is the utilization of plant based polyphenols for the inhibition of the above said enzyme.

1.1 Cholesterol esterase

Cholesterol esterase is a polymeric enzyme that is produced as a component of the pancreatic juice by acinar cells of pancreas [1]. The human body cannot absorb the cholesteryl esters in the diet and thus, cholesterol esterase in pancreatic juice play a vital role in the hydrolysis of cholesteryl ester to cholesterol and free fatty acids. The formed unesterified cholesterol can then be easily absorbed by the intestine into the blood stream. The gene that encodes for cholesterol esterase consists of 11 exons and 10 introns with a length of 9.2 Kb [2]. The cholesterol esterase is a glycoprotein with a molecular weight of 65-69 kDa [3] with 747 amino acids. The active sites are S194, H435, and D320. Thus, the function of cholesterol esterase is to control the bioavailability of cholesterol from dietary cholesterol esters and to aid in transport of free cholesterol to the enterocyte.

Fig -1: Action of cholesterol esterase on cholesteryl ester

2. MEDICINAL PLANTS AND ITS IMPACT

Medicinal plants normally produce different types of secondary metabolites / phytochemicals that are important to cure or prevent a disease and also to defend the attack by various types of microorganisms and insects. Out of 350,000 plant species identified so far, about 35,000 are used worldwide for medicinal purposes and less than about 0.5% of these have been chemically investigated [7]. In the year 2001, about 122 different compounds identified for the treatment of various ailments are derived from the traditional medicinal plants [12]. According to WHO, 80% of the modern drugs are derived from the herbs and plants.
Any part of the plant can possess the medicinal value; this includes the stem, leaves, bark, flower, peel, flesh of the fruit and root. The medicinal uses of some Indian plants have been tabulated below:

### Table 2.1: Medicinal plants and its uses

<table>
<thead>
<tr>
<th>S.N</th>
<th>Common name</th>
<th>Botanical name</th>
<th>Part of the plant</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Chameleon Plant</td>
<td><em>Houttuynia cordata</em></td>
<td>Leaf extract</td>
<td>Dysentery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rhizome</td>
<td>Stomach ulcer</td>
</tr>
<tr>
<td>3.</td>
<td>Elephant foot yam</td>
<td><em>Amorphophalus paeonifolius</em></td>
<td>Corm</td>
<td>Treatment of Bronchitis, asthma, abdominal pain, emesis, dysentery, enlargement of spleen, piles</td>
</tr>
<tr>
<td>4.</td>
<td>South-Indian Uvaria</td>
<td><em>Uvaria narum</em></td>
<td>Root and leaves</td>
<td>To treat intermittent fever, biliousness, jaundice, rheumatic fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Root bark</td>
<td>To control fits during the time of pregnancy</td>
</tr>
<tr>
<td>5.</td>
<td>Kumarika</td>
<td><em>Smilax ovalifolia</em></td>
<td>Root</td>
<td>Venereal disease, urinary complaints and dysentery</td>
</tr>
<tr>
<td>6.</td>
<td>Malabar chloroptum</td>
<td><em>Chlorophytum malabaricum</em></td>
<td>Root</td>
<td>Diuretic</td>
</tr>
<tr>
<td>8.</td>
<td>East Indian arrow root</td>
<td><em>Curcuma anhustifolia</em></td>
<td>Whole plant</td>
<td>Used as non-irritating diet in certain chronic diseases.</td>
</tr>
<tr>
<td>9.</td>
<td>Turmeric</td>
<td><em>Curcuma longa</em></td>
<td>Rhizome</td>
<td>Anti-inflammatory, antitumor, antioxidative</td>
</tr>
<tr>
<td>10.</td>
<td>Opium poppy</td>
<td><em>Papaver somniferum</em></td>
<td>Dry opium</td>
<td>Analgesic, astringent, antispasmodic</td>
</tr>
</tbody>
</table>

### 3. SECONDARY METABOLITES

Plants produce large number of compounds that are required for their survival. These compounds are classified as primary and secondary metabolites. Generally, the secondary metabolites defend the plants against predators and help the plant to withstand the abiotic stress and some are pheromones that attracts insect for pollination. These secondary metabolites have medicinal value and include alkaloids, terpenoids, glycosides, polyphenols, phenolic acid, phenazines, polyketides, saponin, etc.

Alkaloids are nitrogen containing chemical compounds that are produced by the medicinal plants. The alkaloids may be colored or colorless and some are volatile. The alkaloids are produced by 10 – 25% of the higher plants. Nicotine, berberine, cyclopamine, Lupinine are some of the examples of plant alkaloids. Many drugs are produced by the structural modifications of alkaloids. Applications of certain alkaloids are: Ajmaline and quinidine have antiarrhythmic property, vinblastine and vincristine have the antitumor property, morphine has analgesic property, emetine is used as antiprotozoal agent, and anabasine is used as insecticide [19].
3.1. POLYPHENOLS

Polyphenols present in fruits and vegetables are the one that contribute the taste, color, odor and astringency. Thus fruits like pears and berries have 200-300 mg polyphenols/100 g fresh [26]. They have beneficial effects on human health such as protection against cancer, osteoporosis and cardiovascular diseases. On the basis of number of phenol rings they are classified as flavonoids, phenolic acids, lignans, stilbenes.

i) Phenolic acid:

The phenolic acids are aromatic compounds that maybe benzoic acid derivative or cinnamic acid derivative. Phenolic acid are found in coffee, dry fruits and berries [27]. In plants they stimulate the production of IAA and act as signalling molecules [28]. Caffeic acid, ferulic acid, sinapic acid, benzoic acid and gallic acid are the kind of phenolic acids that are found in plants. They protect the plants from the predator microorganisms that contribute to their antimicrobial and antioxidant property. They induce apoptosis, regulates carcinogen metabolism and inhibits DNA binding and cell adhesion [29].

ii) Flavonoids:

Flavonoids are non-nitrogenous polyphenols with the basic structure of two aromatic rings (C6) and one heterocyclic ring which contain an oxygen atom. They play a vital role in floral pigmentation which is crucial to attract pollinators and some inhibit the growth of microorganism. They are classified as flavonols, flavones, flavanones, anthocyanins and isoflavones. They have various properties such as antimicrobial, anti-inflammatory, anti-ulcer, anti-thrombotic, antioxidant, anticancerous and cardiotonic property. In addition they can lower the cholesterol level and can protect liver from hepatitis.
value of 2.54 and 1.70 mg/ml, respectively [34]. Camellia sinensis have also been reported to inhibit the CEase. This is due to the presence of polyphenols i.e., flavonoids. The flavonoids irreversibly bind with the enzyme in its active pocket at serine 194. The effective inhibition is due to the ability of flavanoids to act as substrate ahead of cholesterol esters [35]. Thus, polyphenols from various fruits such as grapes, Hibiscus sabdariffa, Moringa oleifera, etc have the ability to inhibit CEase.

5. CONCLUSION

There are various methods or treatment to prevent hypercholesterolemia and related cardiovascular diseases. The use of chemical drug is effective but may equally have a side effect. Hence, the natural means of inhibition is preferable. One such natural method is the use of polyphenols from various plant sources to inhibit the pancreatic cholesterol esterase. The secondary metabolites i.e. polyphenols prevents the hydrolysis of dietary cholesteryl esters by binding to the active sites of CEase and leads to the prevention of various cardiovascular diseases.

REFERENCES

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