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## Plant secondary metabolites as potential usage in regenerative medicine

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### ABSTRACT

Plants secondary metabolites have shown a potential usage to treat infections, health disorders, and illness. During the years these had been slowly replaced by other synthetic drugs. Many of these higher plants and their products are major sources of useful in different industries such as pharmaceutical, agrochemical, flavor and other aroma industries. On a worldwide scale, medicinal plants which use secondary metabolites mainly uses as crude drugs and extracts to treat diseases. Several of the plant secondary metabolites have a potent usage from these isolated compounds as including alkaloids such as morphine (pain killer), codeine (antitussive), papaverine (phosphodiesterase inhibitor), ephedrine (stimulant), ajmaline (antiarrhythmic), quinine (antimalarial), reserpine (antihypertensive), galanthamine (acetylcholine esterase inhibitor), scopolamine (travel sickness), berberine (psoriasis), caffeine (stimulant), capsaicin (rheumatic pains), colchicine (gout), yohimbine (aphrodisiac), pilocarpine (glaucoma), and various types of cardiac glycosides [1]. Flavonoids such as anthocyanins (antidiabetic), Naringin (anti osteoporotic), Cocoa flavonols (coronary artery disease), cardamonin(anti-cancerous) helps in treating various diseases.

**Keywords:** Alkaloids, Terpenes, Alzheimer, Diabetes, Malaria, Cancer, Coronary heart disease, Flavonolsn.

### INTRODUCTION

The different studies focusses on plant secondary metabolites over the recent years, the secondary metabolites from plants are a great source in pharmaceuticals. These are produced in plants for defense from the external environment [2]. During the times when the plant cell culture came to a led, it emerged as a possible tool for production of secondary metabolites. Different strategies involved from the past for using in-vitro systems had extensively led to the objective of improving the production of secondary plant compounds [3]. Plant secondary metabolites are produced throughout the plant's life cycle. Secondary metabolites are thus an interesting target for plant breeding. The genes associated with the synthesis and production of plant secondary metabolites were isolated and studied pathway at its genetic level. The study revealed that secondary metabolites interact with another for their production [3]. Most of the pharmaceutically produced secondary metabolites derived from plants and their different parts have been utilised. These include mainly alkaloids, glycosides, flavonoids, volatile oils, tannins, resins, etc. [2]

Much of the molecular medicine practiced today involved the use of tissue targets that would exist for each of the small molecules to intervene in diseases and prevent major side effects. The majority of the plant metabolites are used a regenerative medicine are specific in their action. For example, *Withania somnifera*, commonly known as Ashwagandha, has a potential medicinal value and used to treat different diseases indigenously. It has varied sage and the growing therapeutic values which had emerged successfully and considerably in modern scientific attention. The major constituent of *Withania* genus, called the withanolides, and secondary metabolites derived steroidal compound with C28-steroidal lactone triterpenoids linked to form a six-membered lactone ring. It presents to show biological activity in by focusing all two novel activities, like one showing the great impact in curing tumors and its antiangiogenic properties in Alzheimer patients [7].

This review article will provide information about different plant secondary metabolites and their usage as regenerative medicine. Also, their importance in usage for curing diseases has been mentioned which their mode of action and reactions.

### ALKALOIDS

Alkaloids are a class of naturally occurring organic plant compounds which shows neutral and weakly

acidic properties. Alkaloids are being produced by a many number of organisms including bacteria, fungi, plants, and animals [4, 5]. Alkaloids produced from having a wide range of pharmacological activities including antimalarial (quinine), antiasthma (ephedrine), anticancer (homoharringtonine), vasodilatory (vincamine), antiarrhythmic (. quinidine), analgesic (morphine), antibacterial (chelerythrine), and antihyperglycemic activities (e.g. piperine). Many have of the compounds have several different properties which are found usage in traditional or modern medicine, the discovery of the properties has found have the basis for drug discovery

### 1. Treatment of Diabetes

Alkaloids isolated from *Catharanthus roseus* (periwinkle), includes leurosine, vindoline, vindoline and catharanthine, have shown to exhibit a mild hypoglycaemic effect within 2-5 h in healthy rats when it is injected. But this was later found to have cytotoxic effect diabetes patients [4]. On NIIDM patients, the use of leaves from the *Tecoma stans* for the treatment, supported the production of other two other hypoglycaemic alkaloids such as tecomine and tecostanine [5]. These alkaloids have studied to exert a rapid hypoglycaemic effect when administered intravenously to healthy and alloxan-induced diabetic rabbits but were ineffective in pancreatectomies rabbits. But these alkaloids showed poor stability in clinical tests.

Trigonelline another plant alkaloid, chemically known as N-methylnicotinic acid extracted from *Trigonella foenum-graecum* has known to have therapeutic effects to cure hypoglycaemic and hypolipidemic properties [6]. This alkaloid has shown a considerable effect on transcriptional activities. Trigonelline can be been used clinically for the treatment of diabetes and its complications on central nervous system disease, further studies were required, especially to understand the mechanism of action [6].

### 2. Treatment of Neurodegenerative Diseases

Another drug used as the regenerative medicine was Berberine, an isoquinoline alkaloid from the *Coptidis Rhizoma* extract has been shown to have therapeutic potential on central nervous system disorders such as Alzheimer's disease, cerebral ischemia, and schizophrenia [7]. These promote the survival and differentiation of hippocampal precursor cells. This also helps in the increasing the thickness of remyelinated axons when administered which indicates the neurine extension and axonal regeneration in case of injured nerves diseases like myasthenia gravis, lupus, and inflammatory bowel disease [7]. Fig 1

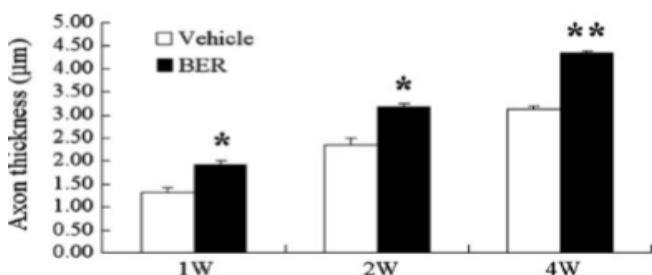


Figure 1: Thicknesses of myelinated axons were increased by BER treatment (20mg/kg) in the distal stumps of injured rat sciatic nerves.

Songorine is an aconite alkaloid which is C<sub>20</sub> diterpenoid alkaloid with the 12-keto analog of napelline, isolated from *Aconitum soongaricum* and was associated with many panels for biological activity [8]. Songorine is found be one of the well-studied secondary metabolites alkaloids and had reported exhibiting dopaminergic cure but the effect in synaptic transmission in mice and it also found to block the effect of bulbocapnine, which is a dopamine receptor antagonist. It was also involved in the anti-inflammatory reaction which was confirmed using carrageenan-induced inflammatory assay [9]. The mechanism of wound

healing was studied for the regenerative effects in the mouse. It specifically involves the regeneration of mesenchymal precursor cells.

### 3. Treatment of Cancer

Vincristine is an alkaloid isolated from the leaves, bark, or stem of (*Catharanthus roseus*). It is proven to have be an oncolytic alkaloid used for the treatment of many different types of cancers [10]. It has also been used and administered along with other antineoplastic drugs such as Hodgkin's disease, sarcomas of specialized structures, breast cancer, and cancer of the uterine cervix and other forms of tumour [10].

### TERPENES

Terpenes are the naturally occurring plant secondary metabolite compounds from different kingdoms of organism such as plant, fungi, animals and bacteria. These constitute most the largest class of naturally occurring compounds. The terpenes are synthesized in plants for pigmentation as in chlorophyll or as a plant growth hormones such as auxin, gibberellin, abscisic acids they have shown to have many pharmacological properties and are preventive against cancer, microbes, fungi, virus, and parasitic.

#### 1. Treatment of Malaria

Artemisinin is one of the important terpene secondary metabolite obtained from the *Artemisia annua* from the shrubs, it has impeccable results in curing malaria. They counter the threat by providing resistance to parasite resistance *Plasmodium falciparum* to different therapies which have the combination of antimalarial [11]. Artemisinin has in the rapid dismiss of symptoms of malaria with the combination of several different drugs. This has been found to have a serious effect on the vector-borne disease caused by *Plasmodium vivax*, *Plasmodium falciparum*, and *Plasmodium malaria*. This derivative was found to have effects by interfering with the effects of haem by producing the carbon centre molecules to alkylate the protein membrane by destroying the insect parasite. Artemisinin has a far-reaching impact and the best alternative in curing malarial diseases [11].

#### 2. Treatment of Body Endurance

Tetrahydrocannabinol is one of the terpenes extracted *Cannabis sativa*, cannabinoids have been studied widely in animals and humans for their effects. These have shown many properties as usage in drugs for nausea, appetite, pain relief, sedation, lethargy, and insomnia [12]. It has provided that Medical Cannabis (MC) use for it as a preferred alternative for the person having seeking rehabilitation from excessive smoking, drinking and drug usage.

### FLAVONOIDS AS REGENERATIVE MEDICINE

Flavonoids are a major class of plant secondary metabolites made up of polyphenolic structures. They are found in all parts of the plants. They are classified into six classes such as anthocyanins, chalcones, flavanones, flavones, flavonols, and isoflavonoids. Flavonoids have various health-promoting effects like antioxidative, anti-inflammatory, anti-carcinogenic and antimutagenic. Hence it serves as an important constituent in pharmaceutical, nutraceutical and cosmetics industries [13]. Flavonoids have antioxidant effects associated with various diseases like Alzheimer's Disease, Cancer, atherosclerosis, etc, [14].

### ANTHOCYANIN

#### 1. Treatment of Diabetes and Diabetes and Diabetes Retinopathy

Cyanidin obtained from sweet potato was tested in human leukemia HL-60 cells and was proved that it has antioxidative, antimutagenic and antiproliferative properties [15]. Anthocyanin-rich pulps have antioxidant properties by which the free radicals associated with diabetes get neutralized [16]. Sour cherries are rich in anthocyanin. Studies showed the lowering effects of blood sugar in Diabetes by

testing various cherries like yellow cherries, sweet cherries and sour cherries [17]. Researchers found that an extract isolated from the seeds of the sour cherry has antidiabetic property [18]. Varga and his colleagues studied the blood sugar levels in Zucker diabetic fatty rats after treating it with sour cherry seed extract. They found that the extract has significant blood sugar lowering effects [19]. Varga and his group studied the effect of sour cherry seed extract on the diabetic eye and found that the extract minimized the severity of high blood glucose and it protects the retina from ischemia-reperfusion injury [19].

## 2. Treatment of Cardiovascular Disease

Adequate uptake of anthocyanin-rich fruits which contains plant bioactive compounds plays an important role in improving blood pressure, endothelial function and insulin sensitivity [20-24]. Hence, Flavonoids are important components of fruits which is responsible for reducing the risk of cardiovascular disease [23]. Anthocyanin-rich foods help in reducing the systolic and diastolic pressure and also changes the arterial stiffness [24]. Anthocyanins have an anti-inflammatory effect on patients with hypercholesterolemia [25]. Earlier studies had been focused on the relationship between flavonoids and cardiovascular disease in women. Younger women with a higher intake of anthocyanin will have reduced risk of myocardial infarction [26]. Higher intake of fruits rich in anthocyanin and flavonoids reduced the risk of myocardial infarction and ischemic stroke in men [27].

## 3. Treatment of Atherosclerosis

Atherosclerosis is characterized by micro-inflammation, the formation of plaques rich in lipoprotein and prothrombotic status. The extracts of cornelian cherry have anthocyanins and other active compounds [36]. The extracts of these fruits are rich in polyphenolic compounds, which has a wide range of pharmacological effects like antiparasitic, anticancer, antiatherosclerotic, neuroprotective, renal protective properties [37].

Cornelian cherry is said to be a most promising source in fighting against atherosclerosis [38].

## FLAVANONES

### 1. Treatment of Bone Disorders

Naringin has osteoinductive properties and researches had been done on integrating the autogenous bone graft in the skull of the rabbit [28]. Naringin preserves the concentration of calcium in bones and it increases the antioxidant activity thereby affecting the quality of bones. Animal studies showed that naringin also has antiosteoporotic activities due to which it suppresses osteoclast formation [29-30]. Naringin induces the secretion of a cytokine receptor called osteoprotegerins which is a promising drug against osteoporosis and it also inhibits osteoclast formation [31].

## FLAVONOLS

### 1. Treatment of Coronary Artery Disease

Dietary flavanols are used as a major protectant of cardiovascular function [32]. Wine, cocoa products, tea, fruits, and vegetables are the major flavanol sources in the human diet. Cocoa contains high concentration of flavanols [33]. Studies have been shown that ingestion of cocoa flavanols result in improved endothelial function in healthy individuals and patients with diabetes and coronary artery disease [32]. Cocoa flavanols also improve the endothelial regenerating capacity in patients with coronary artery disease by the mobilization of circulating angiogenic cells [34]. This cocoa flavanol improves the endothelial function in coronary heart disease patients by lowering lowers the levels of circulating endothelial microparticles. Hence, flavanols can improve endothelial integrity [35].

## CHALCONES

### 1. Treatment of Cancer

Chalcone is found in naturally occurring and synthetic compounds and it has many pharmacological activities. Chalcones and their derivatives also have a broad range of pharmacological activities like antioxidant, antimicrobial, anti-inflammatory and anti-tumor actions.

Recent studies found that chalcones have anticancer activity by tubulin polymerization or depolymerization [42-44]. Naphthalene moiety is said to be an anticancer agent which inhibit the tubulin polymerization [45].

Cardamonin, basically found in cardamom spice and also found in any other plants. It is proved have chemo preventive agent in a variety of cancers including breast, gastrointestinal, hematological and colorectal cancers [39].

On screening a number of molecules, finally found that cardamonin inhibits the tumor growth by destroying the breast cancer stem cell population which has been enhanced after treatment of breast cancer cells in vitro and in vivo with poly (I:C) [40].

Cardamonin is a small molecule which plays an important role in inhibiting the cancer stem cells which was enriched by chemotherapeutic drugs. The enrichment of cancer stem cells is prevented by cardamonin when they are simultaneously used with chemotherapeutic drugs. Cardamonin could also inhibit the stem marker gene expression in breast cancer cells. When cardamonin is co-administered with chemotherapeutic drug doxorubicin in a xenograft mouse model, it retards tumor formation by inhibiting the cancer stem cell population [41].

## DISCUSSION

Thus, varied number and classes of plant secondary metabolites have been described and their usage a regenerative medicine was analyzed. Alkaloids represent a wide class of plant secondary metabolites and represent to cure many diseases like diabetic condition hypoglycaemic and hypolipidemic [6]. It also plays an important role in anti-inflammatory reactions by activation of immune power against the pathogen. Terpenes include metabolites such as Artemisinin and Tetrahydrocannabinol, which had a great improvement by providing a natural method as ailments [11]. Another large class of plant secondary metabolite called flavonoids have shown ailment for cancer, diabetes retinopathy, atherosclerosis, bone disorders, and coronary heart diseases. Anthocyanins play a role in reducing the risk of diabetes [19], it also regulates the systolic and diastolic pressure and it reduces the risk of cardiovascular disease [23-24]. Naringin, a flavanone is used as a drug against osteoporosis [31]. Cocoa flavanols reduce the risk of coronary artery disease [32]. Cardomonin, a chalcone has anti-cancerous activity [14].

## CONCLUSION

Thus, the plant secondary metabolites potential usage has been increased and has shown to have better results than synthetic drugs. This plant metabolite product doesn't have any side effects and as compared to other drugs. These have increased in production for the past years and showed a great improvement in curing the many dreaded diseases. Thus, plant secondary metabolites would be an alternative for synthetic and artificial drugs.

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