Available online on 15.05.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Review Article

Anti-inflammatory Natural Compounds from Herbal and Marine Origin

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ABSTRACT

Inflammation is pathologic condition that includes variety of diseases throughout the world. Natural products have shown their effectiveness consistently in medicinal and cosmetic field. According to World Health Organization (WHO) still about 80% of the world population rely mainly on plant-based drugs. In Ayurveda, Siddha, and Unani, utilizing a large number of medicinal plants were used for the treatment of human diseases. Herbal natural sources have ability to synthesize a wide range of phytochemical compounds which shows anti-inflammatory activity. Secondary metabolites such as alkaloids, flavonoids, saponins, coumarins, terpenoids and essential oils have clinically and experimentally shown anti-inflammory properties over the years. With the emerging developments in natural products, the marine environment has been shown to be the source of a great diversity of chemical structures with promising biological activities. Marine organisms and microorganisms have provided a large proportion of the natural anti-inflammatory products over the years. Marine sources includes bioactive compounds from micro-organisms, such as algae, bacteria, cyanobacteria, fungi and small invertebrates, such as sponges, mollusks, tunicates, echinoderms and phytoplankton's. Algal anti-inflammatory phytochemicals have the potential to be used as therapeutics or in the synthesis of structural analogs with profound anti-inflammatory activity with reduced side effects. This review describes anti-inflammatory activity of some secondary metabolites discovered from herbal and marine sources.

Keywords: Anti-inflammatory, Phytochemical, secondary metabolites, Herbal, Marine

Article Info: Received 30 March 2019; Review Completed 08 May 2019; Accepted 12 May 2019; Available online 15 May 2019

Cite this article as:

Saudagar RB, Saokar SN, Anti-inflammatory Natural Compounds from Herbal and Marine Origin, Journal of Drug Delivery and Therapeutics. 2019; 9(3):669-672 **http://dx.doi.org/10.22270/jddt.v9i3.2906**

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INTRODUCTION

Inflammation is defense or protective response of our body to various hazardous stimuli such as allergens and/or injury to tissue and it involves complex array of enzyme activation, mediator release, fluid extravasations, cell migration, tissue breakdown and repair. It is a complex process, which is frequently associated with pain and involves occurrences such as increase in vascular permeability, increase of protein denaturation and membrane alterations.[1] On the other hand, uncontrolled inflammatory response is the main cause of a vast continuum of disorders including allergies, cardiovascular dysfunction, metabolic syndrome, cancer, and autoimmune disease imposing a huge economic burden on individual and consequently on society. [2] There are various functions of inflammation. It is the first step in the healing or repair, Process after some physical or chemical injury or stress. It is a normal bodily function and it is a healthy action when it is controlled. If there no inflammation even a small cut on the finger could lead to death. Inflammation prevents the spread of damaged cells to other areas of the body that could cause secondary problems. There are also some benefits of inflammation such as, destruction of microbes, thereby eradicating infection,detoxification of toxins, clears infections, facilitates in the healing process Repairs damages tissues. [3]

Non-steroidal anti-inflammatory drugs (NSAIDs), steroids and immunosuppressant drugs that have been used conventionally against all forms of inflammatory conditions are associated with adverse effects like ulceration, perforation, gastric irritation, haematochezia, angioedema, hepatic failure, headache, hemolytic anemia, hyperglycemia, osteoporosis, immunodeficiency-related problems, and others.Considering these potential adverse effects of these drugs and their limited ability to provide long-term remission, complementary and alternative medicinal products that are generally considered safe are continuously being explored for their anti-inflammatory potential. [4] We need to apply natural anti-inflammatory factors within medication therapy to achieve increased pharmacological response and the lowest degree of unwanted side effects. Herbal medicines are promoting subjects in medicine. Complementary, alternative, and traditional medicines are

the important source of herbal medication guidance. Medicinal plants have a wide variety of chemicals from which novel anti-inflammatory agents can be discovered.[2]

Not only plants but also there are other sources which are enriched with medicinal properties. Ocean, the enormous ecosystem which covers more than 70% of earth's surface, has the vast variety of marine organisms that produces a number of secondary metabolites with a range of biological functionalities. Marine organisms represent vast, essentially unexploited, resource of natural products. Natural marine products constitute a field of scientific endeavor that in recent years has grown considerably. [5] The marine environment has been shown to be the source of a great diversity of chemical structures with promising biological activities. Microbiological, immunological and toxic agents can initiate the inflammatory response by activating a variety of immunological and cellular mediators. Progression of inflammatory processes correlates with the release of these cell-derived mediators from the local site of inflammation. These mediators include prostaglandins, leukotrienes, nitric oxide, tumor necrosis factor and cytokines of the interleukin families. [6]

Marine algae have been one of the richest and most promising sources of bioactive primary and secondary metabolites. They synthesize a variety of compounds such as carotenoids, terpenoids, xanthophylls, chlorophyll, vitamins, saturated and polyunsaturated fatty acids, amino acids, acetogenins, polyphenols, alkaloids, and polysaccharides. [5] Various natural products from marine algae were revealed in widely spectral bioactivities, including anti-coagulant, anti-viral, anti-oxidant, anti-allergic, anti-cancer, anti-inflammatory, and anti-obesity activities. [7] Marine organisms include green algae, brown algae, red algae, sponges, fungi, moulds, coelenterates, bryozoans, tunicates, echinoderms, miscellaneous marine organisms and marine microorganisms and phytoplankton. Therefore, the discovery of novel anti-inflammatory drugs from marine source could bring a new insight to the field of biomedical research and industry. This article describes current progress in the development of a selection of new anti-inflammatory agents from marine sources.

SOME SECONDARY METABOLITES THAT HAS AN ANTI-INFLAMMATORY PROPERTIES

1. Flavonoids-

Flavonoids are polyphenolic compounds that occur in foods of plant origin. There are number of different flavonoids have been described, and they are grouped into flavonols, flavones, catechins, flavanones, anthocyanin's and isoflavonoids. They have been shown to exert antimicrobial, antiviral, anti-ulcer genic, cytotoxic, anti-neoplastic, antihypertensive, mutagenic, anti-inflammatory, antioxidant, anti-hepatotoxic, and antiplatelet activities.[8]

2. Alkaloids-

Some alkaloids such as isoquinoline, indole and diterpene are known to have good anti-Inflammatory activity. For example, three types of isoquinoline alkaloids were detected in the roots, barks and branches of Turkish *Berberis*species. Tobacco (*Nicotianatobaccum)* or *tea (camellia sinensis)* have greater proportion of alkaloids in their leaves. Strychnine from *nux vomica* and caffine from coffee contains alkaloids in seed.[9]

3. Sterols-

Phytosterols and their derivatives areimportant components of plant biological membranes. They arealso known as plant sterols, are cholesterol-like molecules found in plants such as whole grains, fruits, legumes (e.g., lentils and soybeans), and other vegetables and are biogenetic precursors of numerous metabolites such as plant steroid hormones. Plant sterols have been investigated as an alternative for lowering plasma cholesterol levels, and several studies have shown that they significantly reduce plasma total and low density lipoprotein cholesterol. Plant sterols have been shown to have other metabolic effects. There are insufficient evidences for heart attack, obesity, colon tumors etc. [4]

4. Phenolic compounds-

Phenolic compounds are of important pharmacological value, some of them having anti-inflammatory properties. Different types of phenolic compounds such as flavonoids, condensed tannins, and Gallo tannins are known to inhibit some molecular targets of pro-inflammatory mediators in inflammatory responses.The most common phenolic acids in plant tissues are hydroxycinnamic acids.[9]

5. Coumarins-

Coumarins represent a vast family of compounds which are naturally occurring in plants. It has been already reported that several coumarin derivatives have significantly anti-inflammatory property. [10] For example, Cedrecoumarin A is a compound found in african plant *Cedrelopsis longibracteata* (Ptaeroxylaceae) has an antiinflammatory property. 6-Hydroxy-7-methoxy coumarin or scopoletin is a compound produces by *Scaphopeta lumthonneri* (Sterculiaceae) and *A. majus*L. (Apiaceae) plant has anti-viral, anti-inflammatory and anti-microbial activity.[11]

6. Terpenoids and Essential oils-

Essential oils are natural, volatile complex compounds usually having a strong odour and are formed by aromatic plants as secondary metabolites. Not all plants produce enough essential oil to justify the commercial cost of extracting the oil. They are called terpenes, and they occur as diterpenes, triterpenes, and tetraterpenes, as well as hemiterpenes and sesquiterpenes. If the compounds contain additional elements, usually oxygen, they are termed terpenoids. Examples of common terpenoids are curcumin, menthol and camphor.[12]

7. Saponins-

Saponins are steroid or triterpene glycosides enourmously found in the plants that include a large number of biologically active compounds. Saponins decrease the absorption of food in digestive track and hence it is used in slimming diet. Examples of saponin rich plants are asparagus (*asparagus officinalis),* alfalfa *(medicago sativa)*. [11]

ANTI-INFLAMMATORY COMPOUNDS FOUND IN THE MARINE ENVIRONMENT-

1. Peptides and proteins

Marine environments are a well-established source of unique and anti-inflammatory active peptides. Complex cyclic peptides and depsipeptides have emerged as an important class of metabolites present in extracts of marine organisms and microorganisms. For example, cyclomarins A-C are new anti-inflammatory cyclic peptides produced by the marine bacterium *Streptomyces* spp. marine organisms have been reported to produce anti-inflammatory active proteins, which are probably involved in the protection of organisms against physiological and stress conditions. The marine protein has been shown to be a potent dual inhibitor of human secretory and cytosolic PLA2 with anti-inflammatory activity.[6]

2. Phospholipids

Marine fatty acids are of interest for the different role and biological properties they exhibit in the cells of marine organisms. Sphingolipids, Galactoglyco sphingolipid, sulfoglycolipidare the lipids isolated from marine sources.[7]

3. Polysaccharides

Cell walls of the red algae contain large amount of sulfated, water-soluble polysaccharides, with varying levels and patterns of substitution by sulfate, methoxy, pyruvate groups or sugar side chains. polysaccharides showed interesting anti-inflammatory properties. Sulfated polysaccharides from red microalgae have anti-inflammatory activity.[13]

4. Macrolides

Macrolides are a group of compounds containing a macrocyclic lactone ring, and up to 9 conjugated transdouble bands. Macrolides constitute an important class of natural anti-inflammatory products of marine origin, especially from marine bryozoa. The bryostatins are a unique family of emerging anti-inflammatory candidates isolated from marine bryozoa. They were first discovered in the bryozoan *Bugulaneritina*.[6]

5. Other compounds

Terpenoids, steroids, alkaloids and phenolic compounds are also found in marine sources such as red algae, brown algae, sponges, fungus and other micro-organisms.[14]

PLANTS WITH ANTI-INFLAMMATORY ACTIVITY

Swertia chirata (Gentianaceae) is an ayurvedic therapeutic plant. The ethanolic extract of *swertia chirata* reduced the inflammation and pain. It is an effective medication for weak stomach, particularly when itresults in indigestion, bloating and nausea. In addition, this bitter tonic and effective in protecting the liver and it is also beneficial in treatment of malarial fevers. [15]

***Emblica officinalis* (Euphorbiaceae)**

The *Emblicaofficinalis*using carrageenan and cotton pellet induced acute and chronic inflammatory animal model. The compounds were studied for their acute and chronic anti-inflammatory activity at a dose level of 20 and 40 mg/kg against standard drug diclofenac. The results indicated that in both acute and chronic reduction in the inflammation, but significant effects were observed only at high doses. [10]

***Albizialebbeck*(Mimosaceae)**

The juice of *albizialebbeck* leaves used to treat night blindness. Bark and seeds possess astringent activity. Also use to reduced diarrhoea, dysentery and haemorrhoids. Flowers are used as emollient to sooth eruption, burns and swellings. It also shows an anti-inflammatory property. [16]

***Cassia occidentalis*(Fabaceae)**

Whole plant of *Cassia occidentalis* using ethanolic extract has shown significant reduction in carrageenan induced inflammation in mice at a dose of 250 mg/kg. Its roots decoction is used in the treatment of urinary retention and inflammatory conditions. Leaves are used in asthma and chronic respiratory disorders. It is also helpful in cases of cough, cold, eczema, dyspepsia and constipation. [7]

***Rosmarinus officinalis*(Lamiaceae)**

Rosemary is native in the mediterranean area. It is an oldest known medicinal herb. Extracts and the volatile oil have been used to promote menstrual flow. Rosemary also may reverse headaches, reduce stress, and aid in asthma and bronchitis treatment and has an antioxidant action. In a preclinical study on rats, high dose of rosemary extract (500mg/kg) has shown reduced testosterone and spermatogenesis level that led to infertility. This plant has had topical anti-inflammatory in wound healing property. [2]

ANTI-INFLAMMATORIES OF MARINE ORIGIN

***Spirulina* (Arthrospira)**

Spirulina, a filamentous unicellular alga, is a cyanobacterium used in certain countries as foods for human and animal consumption; is one of the most extensively studied from the chemical, pharmacological and toxicological points of view. Spirulina has rich amount of protein, essential and non-essential amino acids, also has high levels of gamma-linolenic acid (GLA), beta-carotene, arachidonic acid, vitamin B12, minerals iron, calcium, phosphorus. Dietary supplementation of *Spirulina*has helped in alleviating the incidence of anemia experienced during pregnancy and lactation. [14] *Spirulina* was effective in decreasing IgE antibody level and increasing IgG1 and IgA antibody production in the serum of the mice immunized with crude shrimp extract as an antigen. It has anti-inflammatory and antioxidant activity. [5]

Marine algae

In sponges, an acetylated nitrogenous glycolipid 554 was isolated from *Plakinastrellaclathrata* with the absolute configuration confirmed by synthesis of lipidchain analogues. The compound was claimed to be a moderate anti-inflammatory by inhibition of PGE_2. Anti-inflammatory active phenolic compounds isolated from *Eisenia bicyclis* are phloroglucinol, eckol, dieckol, 7-phloroeckol, phlorofucofuroeckol A and dioxinodehydroeckol which cause Inhibition of LPS-induced nitric oxide (NO) production in cells. Vidalols A and B isolated from *Vidalia obtusaloba* causes inhibition of mouse ear inflammation induced by phorbol ester through inhibition of phospholipase A2. Fucoidans is alsoa polysaccharide isolated from nine different brown algae shows leucocyte recruitment in rats. [17]

Alginic acid is a polysaccharide isolated from *Sargassum wightii* provides anti-inflammatory potential against adjuvant-induced arthritis, reduced paw edema in rats with reduction of activity of cyclooxygenase, lipoxygenase and myeloperoxidase enzymes and C-reactive protein, ceruloplasmin and rheumatoid factor levels. Sulfated galactofucanis also a polysaccharide from *L. variegate* causes inhibition of ear swelling induced by croton oil by inhibitingleukocyte migration. Stearidonic acid and timnodonic acid are fatty acid and lipid derivatives isolated from Undaria pinnatifida shows inhibition of mouse ear inflammation induced by phorbol myristate acetate. *Dunaliella bardawil* is a marine algae which synthesize an anti-inflammatory active terpenoid called Beta-carotene which shows protective activity against acetic acid-induced small bowel inflammation through the suppression of mucosal myeloperoxidase activity. Sargachromanol G is anti-inflammatory compound isolated from *S. siliquastrum* shows the anti-inflammatory effect of LPS stimulated cells through the reduction of NO production and iNOS, PGE2 and COX-2 production. [13] The Caribbean sea whip, Pseudopterogorgiaelis- abethae L. (Octocorallia, Cnidana), has been found to contain pseudopterosins, which have been characterized as diterpenepentose glycosides. pseudopterosins possess anti-inflammatory and analgesic properties that exceed the potencies of existing drugs such as indomethacin.[18]

CONCLUSION

Natural products play an important role in prevention and/or treatment of inflammatory and allergic diseases Herbal natural sources like plants have played an important role in the discovery of new drugs. Synthetic drug formulations can cause various harmful side effects to human beings. A large number of unique and potential anti-inflammatory compounds have been isolated from marine sources.The phytochemical and medicinal compounds isolated from herbal and marine sources play a vital role in the pharmaceutical industry in future to develop novel drugs against inflammatory and various other disorders.

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