POTENT ULCER PROTECTIVE ACTION OF ANTI-INFLAMMATORY HERBS: A SHORT REVIEW

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ABSTRACT
Rheumatoid arthritis (RA) is an autoimmune, symmetrical polyarticular disease that affects primarily the diarthrodial joints, which is characterized by chronic inflammation of the synovial joints. The measure antirheumatic drugs used in the treatment of RA are non-steroidal anti-inflammatory drugs (NSAIDs) DMAD’s, biological agents and others. The NSAIDs utilized in treatment of inflammation are one the most widely used classes of drugs throughout the world, but their undesirable side effects on gastric mucosa and cardiovascular system are well known. However, NSAID’s, despite their great number, their therapeutic efficacy seems to be hampered by the presence of a number of undesired and often serious side effects.

Recently, there has been much interest in natural medicines derived from the traditional knowledge of plant pharmacological properties. Large number of medicinal plants and dietary nutrients has been shown to pose gastro-protective activity and anti-inflammatory activity. Present study highlighting comprehensive review on herbal drugs showing both anti-inflammatory and potent gastro-protective effect.

KEY WORDS: Rheumatoid arthritis, Inflammation, Antiinflammatory, Gastroprotection, Herbal drugs, Phytotherapy.

INTRODUCTION
Rheumatoid arthritis (RA) is an autoimmune, symmetrical polyarticular disease that affects primarily the diarthrodial joints, which is characterized by chronic inflammation of the synovial joints. The pathogenic characteristic features of RA includes synovial hyperplasia
and inflammation accompanied by cartilage loss and joint destruction which results in extremely painful, impaired functional status, and produces substantial morbidity as well as an increase in mortality \cite{1, 2}. The measure antirheumatic drugs used in the treatment of RA are non-steroidal anti-inflammatory drugs (NSAIDs) DMAD’s, biological agents and others. The NSAIDs utilized in the treatment of inflammation are one the most widely used classes of drugs throughout the world, but their undesirable side effects on gastric mucosa and cardiovascular system are well known \cite{3-5}. Therefore, the search for more effective anti-inflammatory drugs is still very relevant. The use of plants as medicine dates back to early man \cite{6}. Often this folk medicine is the only source of access for certain populations for treating their diseases \cite{7}. However, the traditional use of plants is not sufficient for ethical validation of their therapeutic effects, requiring scientific studies to verify their real pharmacological potential \cite{8}.

Gastric hyperacidity and ulcer are very common cause of human suffering today. It is an imbalance between damaging factors within the lumen and protective mechanisms within the gastro duodenal mucosa. Although prolonged anxiety, emotional stress, hemorrhagic surgical shock, burns and trauma are known to cause severe gastric irritation, the mechanism is still very poorly understood \cite{9}.

The classical description of inflammation accounts for the increases in the number of leucocytes and a variety of complex mediator molecule \cite{10}. Prostaglandins are ubiquitous substances that indicate and modulate cell and tissue responses involved in inflammation. Their biosynthesis has also been implicated in the pathophysiology of cardiovascular diseases, cancer, colonic adenomas and alzheimer’s disease \cite{11}. There are various components to an inflammatory reaction that can contribute to the associated symptoms and tissue injury. Oedema formation, leucocyte infiltration and granuloma formation represents such components of inflammation \cite{4}. Traditionally, the treatment for inflammation has been to use a (NSAIDs), such as aspirin, for pain relief and to use corticosteroids or even disease-modifying drugs in an attempt to reduce other symptoms of the disease. However, NSAID’s, despite their great number, their therapeutic efficacy seems to be hampered by the presence of a number of undesired and often serious side effects \cite{1}. Recently, there has been much interest in natural medicines derived from the traditional knowledge of plant pharmacological properties \cite{12}. 

### Table 1: Details of plants showing both anti-inflammatory and ulcer protection actions

<table>
<thead>
<tr>
<th>Name of plant</th>
<th>Family</th>
<th>Parts used</th>
<th>Extract/ known chemical constituents</th>
<th>Anti-inflammatory model</th>
<th>Ulcer-protective model</th>
<th>Possible mechanism/ outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agave seemanniana</td>
<td>Asparagaceae</td>
<td>Leaves</td>
<td>Methanol extract; saponin fraction</td>
<td>Carrageenan induced paw edema method</td>
<td>Ethanol induced ulcer model</td>
<td>Potent action by their high saponin content [15].</td>
</tr>
<tr>
<td>Albizia chinensis</td>
<td>Fabiaceae</td>
<td>Fruits and bark</td>
<td>Chloroform extract</td>
<td>Carrageenan induced paw edema method</td>
<td>Ethanol induced ulcer model</td>
<td>The extract shows treatment of inflammation and reduced ulcer effects [16].</td>
</tr>
<tr>
<td>Alstonia scholaris</td>
<td>Apocynaceae</td>
<td>Leaves</td>
<td>Dichloromethane and ethylacetate fractions from methanolic extract</td>
<td>Carrageenan induced paw edema method</td>
<td>Pylorus ligation model</td>
<td>Dichloromethane fraction shows potent anti-inflammatory and ulcer protection action [17].</td>
</tr>
<tr>
<td>Aristotelia Chilensis</td>
<td>Elaeocarpaceae</td>
<td>Ripe fruits</td>
<td>Ethanol, acetone, ethylacetate and Methanol/water extracts and subfractions</td>
<td>Carrageenan induced paw oedema method</td>
<td>Pylorus ligation model</td>
<td>Anthocyanins, flavonoids and phenolic acids may be responsible for anti-inflammatory &amp; gastroprotective activities [18].</td>
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<tr>
<td>Byrsonima genus</td>
<td>Malpighiaceae</td>
<td>Stem bark</td>
<td>Decoctions or infusions from aqueous extracts</td>
<td>Carrageenan induced paw oedema method</td>
<td>Pylorus ligation model</td>
<td>Promising anti-inflammatory &amp; gastroprotective activities by the extracts [19].</td>
</tr>
<tr>
<td>Caesalpinia pulcherrima (Linn.) Sw.</td>
<td>Leguminosae/ Caesalpinioideae</td>
<td>Aerial</td>
<td>Ethanol &amp; aqueous extracts</td>
<td>Cotton pellet granuloma model</td>
<td>Pylorus ligation &amp; aspirin induced ulcer models</td>
<td>Plant possesses significant anti-inflammatory &amp; antiulcer activities [20].</td>
</tr>
<tr>
<td>Cuphea aequipetala</td>
<td>Lythraceae</td>
<td>Aerial parts</td>
<td>Infusion; Polyphenols and flavonoid</td>
<td>Xylene &amp; TPA induced ear edema assay</td>
<td>In vitro anti-H. pylori activity &amp; ethanol-induced gastric ulcer model</td>
<td>Promising herb in an integral therapy for the treatment of bacterial or non-bacterial gastric ulcer and anti-inflammatory properties [21].</td>
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<tr>
<td>Calotropis gigantea</td>
<td>Asclepiadaceae</td>
<td>flowers</td>
<td>Chloroform &amp; ethanol extract</td>
<td>Carrageenan induced rat paw edema &amp; cotton pellet induced granuloma model</td>
<td>Pylorus ligation &amp; aspirin induced gastric ulcers model</td>
<td>Both extracts show potent anti-inflammatory &amp; ulcer protection activity [22].</td>
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<tr>
<td>Plant Name</td>
<td>Family</td>
<td>Part</td>
<td>Extract Type</td>
<td>Activity Models</td>
<td>Comments</td>
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<td>Cissus multistriata</td>
<td>Vitaceae</td>
<td>Leaves</td>
<td>Methanol extract</td>
<td>Acetic acid induced edema model, Ethanol induced gastric ulcers model</td>
<td>Both the activity by presence of flavonoids in extracts [23].</td>
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<tr>
<td>Enicostemma littorale</td>
<td>Gentianaceae</td>
<td>Aerial parts</td>
<td>Methanol extract</td>
<td>Inhibition of albumin denaturation (in-vitro), Aspirin induced ulcer and pylorus ligation models</td>
<td>Proves beneficial in arthritic conditions, with no danger of GI distress [24].</td>
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<tr>
<td>Gracilaria changii</td>
<td>Gracilariaceae, Rhodophyta</td>
<td>Red algae</td>
<td>Methanol extract</td>
<td>In-vitro models using Human promonocytic cell line (U937 cells) cell lines, Ethanol induced gastric ulcers model</td>
<td>By elucidating the exact molecular &amp; cellular mechanisms of action, it becomes potent agent for the treatment of chronic ulcers [25].</td>
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<tr>
<td>Pluchea indica</td>
<td>Asteraceae</td>
<td>Root</td>
<td>Methanol fraction</td>
<td>Arachidonic acid, Platelet activation factor &amp; Compound 48/80-induced paw oedema models, alcohol and Indomethacin, induced ulceration &amp; pylorus ligation rat model</td>
<td>Possible 5-LOX pathway of prostaglandin synthesis inhibition [26].</td>
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<tr>
<td>Piper aleyreanum</td>
<td>Piperaceae</td>
<td>Aerial parts</td>
<td>Essential oils</td>
<td>Carrageenan-induced pleurisy model, Acute ethanol-induced lesions in rats method</td>
<td>Showed potential for the development of safe phytomedicine with anti-inflammatory &amp; gastroprotective properties [27].</td>
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<td>Turnera ulmifolia</td>
<td>Turneraceae</td>
<td>Aerial</td>
<td>Hyroalcoholic extract; flavonoids</td>
<td>Carrageenan induced edema, and cotton pellet granuloma model, Indomethacin, alcohol induced ulceration and pylorus ligation in rat</td>
<td>Plant shows beneficial in arthritic conditions, with no danger of GI distress [28].</td>
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<tr>
<td>Tecomaria capensis</td>
<td>Bignoniaceae</td>
<td>Leaves</td>
<td>Ethyl acetate &amp; ethanol extracts</td>
<td>Carrageenan induced paw edema (in-vivo) &amp; HRBC stabilization method (in-vitro), Aspirin induced method</td>
<td>Plant shows beneficial in arthritic conditions, with no danger of GI distress [29].</td>
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<tr>
<td>Achillea millefolium</td>
<td>Asteraceae</td>
<td>Whole Plant</td>
<td>Hyroalcoholic extract</td>
<td>Lipopolysaccharide-induced inflammatory model, Acute gastric lesions induced by ethanol &amp; chronic gastric ulcers induced by 80% acetic acid</td>
<td>The presence of sesquiterpenes is caused by inhibition of arachidonic acid metabolism. And antioxidant properties of may contribute to the gastroprotective activity of this extract [30,31].</td>
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<tr>
<td>Aspilia Africana C.D. Adams</td>
<td>Compositae</td>
<td>Leaves</td>
<td>Hexane extract for anti-inflammatory &amp; aqueous extract for</td>
<td>Xylene-induced ear edema, egg albumin &amp; agar induced paw edema, formaldehyde-induced, Ethanol, indomethacin and aspirin induced ulcer methods</td>
<td>Extract contained sterols &amp; terpenoids responsible for anti-inflammatory action [32]. The presence of glycosides,</td>
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<tr>
<td>Plant</td>
<td>Family</td>
<td>Part Used</td>
<td>Application</td>
<td>Action</td>
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<tr>
<td><strong>Bacopa monnieri</strong></td>
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<td>Whole herb</td>
<td>Aqueous</td>
<td>In-vitro (COX and cytokine estimation) activity</td>
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<tr>
<td>Cistus laurifolius</td>
<td>Cistaceae</td>
<td>Leaves for antiinflammatory; flower &amp; flower buds for ulcer protection</td>
<td>3 flavonoids from ethanol extract: 3-O-methylquercetin3, 7-O dimethylquercetin &amp; 3,7-O-dimethylkaempferol for antiinflammatory &amp; ulcer protection</td>
<td>Carrageenan-induced paw oedema, acetic acid-induced, increased vascular permeability model</td>
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<tr>
<td>Alpinia galangal, Cinnamomum cassia, Cinnamomum tamala, Mentha arvensis, Myrtus communis, Oligochaeta ramose, Polygonum bistorta, Rosa damascena, Ruta graveolens, Syzygium aromaticum, Tamarix dioica, and Terminalia chebula</td>
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<td>Anti-H.pylori activity against Helicobacter pylori strain (193C)</td>
<td>Evaluation of IL-8 secretion &amp; ROS generation</td>
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</tbody>
</table>

Tannins, alkaloids, saponins and flavonoids responsible for antiulcer action \(^{[33]}\).

The drug acts on systemic and brain inflammation driven by the innate immune system \(^{[34]}\). Drug shows good ulcer protection \(^{[35]}\).

Three flavonoids were shown to have strong anti-inflammatory & antinociceptive activities \(^{[36]}\). Active fraction showed a potent anti-acid activity \(^{[37]}\).

These plants showed potent anti-inflammatory & ulcerprotective effects \(^{[38]}\).
TPA, 12-Octadecanoylphorbol-13-acetate; HRBC, human red blood cell membrane; H. Pylori, Helicobacter pylori. GI, gastrointestinal; LOX, lipoxygenase; COX, cyclooxygenase.

Figure 1: Parts of plants (selected) which are showing both anti-inflammatory and ulcer protection actions
Large number of medicinal plants and dietary nutrients has been shown to poses gastro-protective activity and anti-inflammatory activity. The use of traditional medicine is widespread and plants still present a large source of novel active biological compounds with different activities. Phytochemicals are used as templates for lead optimization programs, which are intended to make safe and effective drugs\textsuperscript{[13, 14]}. The details of plants showing anti-inflammatory and ulcer protection actions along with their name of families, parts used, type of extracts including known chemical constituents, methods or models employed for anti-inflammatory and ulcer protection activity and possible mechanism/ outcomes are discussed in table 1.

**CONCLUSION**

The detail study is needed to pinpoint exact mechanism indicating both anti-inflammatory activities with gastric protection effect by each herbal drug and their active constituents. Therefore, this review is having a promising object and further studies are required aiming to support the mechanism of these pharmacological activities. Thus, there remains a tremendous scope for further scientific exploration of these drugs discussed to establish their therapeutic efficacy and commercial exploitation.

**REFERENCES**


