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A REVIEW ON THE ANTISPASMODIC POTENTIAL OF SOME TRADITIONAL MEDICINAL PLANTS OF INDIA

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ABSTRACT: For the treatment of many illnesses and disorders, including gastrointestinal (GI) ailments, several medicinal plants have been used. Most children and adolescents often suffer from GI illnesses, which have overlapping clinical manifestations in diagnosis and treatment requirements. In order to address the symptoms of smooth muscle contraction and cramping in gastrointestinal illnesses as well as in other urgent clinical circumstances, medications having antispasmodic properties are typically used. The treatment of GI illnesses by antispasmodic herbs was a major component of alternative medicine. Due to the numerous nutritional and therapeutic advantages of these medicinal plants and the herbal products they produce, they are utilized from generation to generation. Due to the numerous nutritional and therapeutic advantages of these medicinal plants and the herbal products they produce, they are utilized from generation to generation. The existence of chemical components that are physiologically active may be the cause of the many uses. This review's major objective is to concentrate on the therapeutic potential of plants with antispasmodic properties and their suggested mechanisms of action. A number of databases, including Google Scholar, Cochrane D, Scopus, and PubMed, were utilized to look up relevant articles about "plants with antispasmodic activities." The revised and quantified information on some Indian medicinal herbs with antispasmodic action is highlighted in this study.

INTRODUCTION: The majority of the world's youngsters often complain of gastrointestinal issues, which are prevalent sorts of complaints. In addition to gastroenteritis and acute gastrointestinal illnesses, these conditions include functional abdominal discomfort, ulcerative colitis, irritable bowel syndrome (IBS), infantile colic, and constipation. Disorders of the digestive system can result in a worse quality of life and a higher risk of anxiety and depression¹.

These conditions are characterized by recurring or persistent stomach discomfort, which in IBS is also connected to aggravation, alleviation, or a change in bowel habits². Along with symptoms like discomfort, constipation, or diarrhea, irregularities in intestinal movement are also linked to IBS. People who have diarrhea frequently exhibit symptoms including loose, watery stools³.

Without distinction between male and female patients, IBD is most frequently diagnosed in individuals in the middle of their third and fourth decades of life. About 25% of the afflicted youngsters had a family history of IBD. There have been no recorded differences between healthy and IBD-affected children with regard to some of these characteristics, such as gender, formula intolerance, nursing, emotional stress, or past gastrointestinal

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disease⁴. The gastrointestinal disorder ulcerative colitis (UC) also affects the colon's morphology and has a limited inflammatory response. Histological analysis has shown that crypt abscesses, goblet cell depletion, distortion of the mucosal glands, acute and chronic mononuclear cell-mediated inflammation of the mucosa, polymorphonuclear leukocytes, and mucosal inflammation are some of the symptoms⁵. The oropharynx to the perianal area of the gastrointestinal tract (GIT) may be affected by Crohn's disease, another inflammatory bowel disorder. It has transdermal irritation that could spread to the serosa, which frequently causes the creation of a sinus tract or fistula⁶.

Etiology of Gastrointestinal diseases: Abdominal discomfort, indigestion, constipation, and diarrhea are some of the clinical signs of gastrointestinal diseases, which can be caused by a number of infectious pathways, including aberrant GI motility and decreased GI mucosa barrier. The first possible explanation is the ostensibly increased risk of GI illnesses that overlap and are connected to reflux. The regurgitation of lower GIT contents into the upper region of the GIT is referred to as reflux and functional dyspepsia have both been linked to disturbed motility. In addition, a number of muscles throughout the GIT, including the orbicular iris muscle, ileocecal valve, pylorus,

proventriculus, and opening of the vermiform appendix, Oddi sphincters, and the anus, may serve as gates or checkpoints. All of these checkpoints have smooth muscle or sphincters fixed as barriers that prevent the opening and effacement challenges brought on by lower abdominal contents. If these barriers fail, lower gut juice will reflux into the upper GIT. The first conceivable mechanism is the reflux-related, allegedly increased incidence of overlaps in GI diseases. Reflux is the process by which the contents of the lower GIT are reabsorbed into the upper GIT⁷. Researchers discovered that individuals with injured smooth muscle and sphincter displayed fluctuations in glucose, GI hormones, and free radicals in oxidative stress⁸.

The second pathophysiologic mechanism is GI stimulation that is agitated. Depression, rage, and emotional irritability are common irritable comorbidities in gastrointestinal illnesses⁹. The GI microcirculation's stasis is the third mechanism. Researchers have shown that functional dyspepsia, peptic ulcers, and IBS all have fluctuating catecholamine levels. Additionally, additional investigations have discovered that colitis and IBS have disrupted blood viscosity, which causes an imbalance in myogenic chemometric autoregulation and the stagnation of abdominal circulation¹⁰.

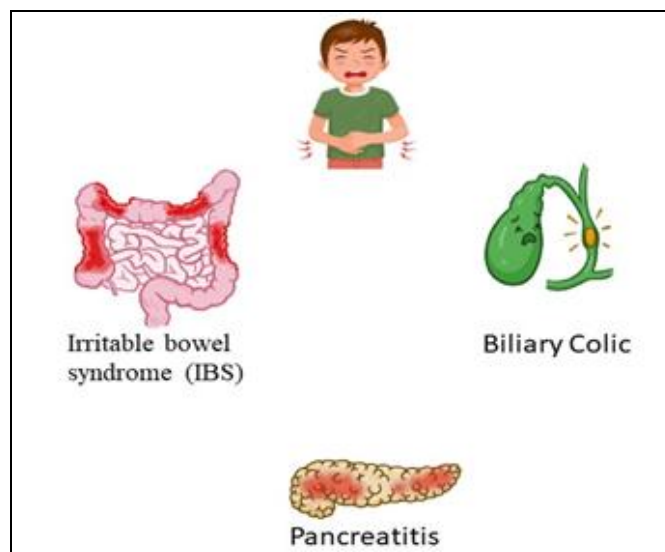


FIG. 1: ETIOLOGY OF GASTROINTESTINAL DISEASE

Traditional Medicine as an Antispasmodic Medication: Traditional remedies have been utilized to treat a variety of disorders since ancient

times. Different plant components are frequently employed in the treatment of various diseases. It has been demonstrated that many therapeutic plants

have fewer adverse effects than manufactured medications¹¹. When compared to manufactured medications, these natural medicinal substances are less expensive and have less hazardous side effects¹². Typical examples of medicinal plants that could be applied as an antispasmodic agent against various GIT disorders like constipation, diarrhea, irritable bowel syndrome (IBS), etc., include *Ephedra*, *Datura stramonium*, *Solanum dulcamara*, *Atropa belladonna*, *Grindelia camporum*, *Hyssopus officinalis*, *Thymus vulgaris*, *Glycyrrhiza glabra*, *Lobelia inflata*, *Marrubium vulgare*, *Euphorbia hirta*, *Coleus forskohlii* and *Inula* are the respiratory spasmolytic. For the treatment of intestinal diseases and menstrual pain, chamomile is an efficient anti-inflammatory and antispasmodic traditional medicine¹³.

According to studies, the plants from the Lamiaceae and Asteraceae families have the most isolated spasmolytic components and the strongest antispasmodic effects. Different mechanisms underlie the activity of antispasmodic herbs techniques such as preventing neurotransmitter release like serotonin, acetylcholine, or 5-hydroxytryptamine via opening potassium ATP channels, decreasing extracellular calcium, muscarinic receptors being blocked, Vanilloid receptors, sodium channels, calcium channels and involvement. Natural products achieve their spasmolytic impact in this way^{14, 15}. Medical plants are used to treat and control a variety of bodily systems and have a wide range of indications. Additionally, these natural therapeutic treatments are important sources of several chemical components that may prove to be future medication candidates. Numerous medicinal plants are employed in the treatment of various GIT problems^{16, 17, 18}. The spasmolytic substances may be found all across nature. To find medicinal plants with antispasmodic potential, a basis of traditional knowledge and ethnobotanical research is provided. Determining 15 historically highly regarded medicinal plants with antispasmodic potential through *in-vitro* and *in-vivo* experiments as well as clinical trials, we are offering measured and updated the information in this area.

***Foeniculum vulgare* Mill:** A perennial herb and flowering plant with feathery leaves and yellow blooms known as fennel is used in traditional

medicine to treat a variety of illnesses. One of the world's oldest medicinal herbs is this one. It has several medicinal benefits, including those that are anti-inflammatory, antibacterial, antispasmodic, apoptotic, galactagogue, emmenagogue, antioxidant, antifungal, antimicrobial, and memory-enhancing. It has been proven that fennel oil significantly reduces the number of tracheal contractions brought on by methacholine in isolated guinea pigs. This could be related to the potassium channel opening. Primary dysmenorrhea is helped by essential oil, which also lessens the discomfort^{19, 26}.

***Atropa belladonna*:** additionally known as belladonna or deadly nightshade, is a toxic perennial herbaceous plant. Alkaloids including scopolamine, atropine, and hyoscyamine are present in its roots and leaves. Children are in serious danger of poisoning from *A. belladonna* since it looks similar to other berries. It is utilized in both homeopathy and allopathy, therefore in allopathy, atropine and scopolamine, which is an extract of *A. belladonna*, and is used to treat colic and induce spasmolytic activity. It inhibits muscarinic receptors, relaxing smooth muscle. Compared to atropine, scopolamine has a stronger antispasmodic action. This plant contains atropine, a well-known anticholinergic chemical. Atropine's antagonistic activity on muscarinic receptors causes the GIT muscle to relax, relieving spasms and inhibiting diarrhea^{27, 28}.

***Anethum graveolens* (Apiaceae Family):** In newborns, antispasmodic and anti-hiccup properties are frequently used in ethnopharmacology. The antiemetic, anti-convulsant, and muscle relaxant properties of this substance. Along with these folkloric remedies, it is also used to treat menstruation issues. For newborns, the common ethnopharmacological applications include antispasmodic and hiccup prevention. It possesses antiemetic, anticonvulsant, and muscle-relaxing properties. In addition to these folkloric practices, it is also used to treat menstruation irregularities. It reduces indigestion, stomachache, and flatulence. It provides a relaxing effect and reduces the discomfort associated with primary dysmenorrhea. On the basis of phytochemical investigation, the presence of quercetin, rutin, flavonoids, isorhamnetin, and their

derivatives in dill has been proven. The quercetin and rutin components found in dill extract have an antispasmodic impact on the rat ileum that has been separated from the rest of the body^{19, 25}.

Ficus carica: In the conventional approach, several components of *Ficus carica*, including fruits, roots, and latex, are utilized. The main chemical byproducts of this medicinal plant are ferulic acid, coumarin, lupeol acetate, sitosterol, and other metals as well as salt, gum, and other substances like salt. *F. carica* is used as an appetizer, an antianemia, an anti-inflammatory, and an antitussive in ethnopharmacology. In addition, it is utilized locally as an antibacterial, constipating, and TB therapeutic agent. Also somewhat laxative, expectorant, diuretic, cytotoxic, and anthelmintic, the herb has several other properties. *F. carica* has reportedly been shown to have antispasmodic properties. A study was conducted on the plant's aqueous-ethanol extract. The experimental work utilized isolated rabbit jejunum preparations^{36, 37, 28}.

Acorus calamus: *Acorus calamus* is an essential medicinal plant used to treat a variety of illnesses, and its primary chemical constituents include alpha-asarone, calamine, methyl eugenol, methyl isoeugenol, and volatile and essential oil. This herb is used to treat skin, vascular, and neurological disorders. Additionally, this herb is utilized to treat digestion and neurological system issues³⁸. Antispasmodic, anti-inflammatory, anti-depressive, antipyretic, antiemetic, expectorant, carminative, tranquilizer and antibacterial are some

of this plant's pharmacological effects³⁹. It has been noted that *A. calamus* has the ability to relax muscles by blocking calcium channels. Using isolated rabbit jejunum preparation, a crude extract of *A. calamus* was tested for antispasmodic efficacy. The use of *A. calamus* prevented high K⁺ (80mm) generated contractions and showed antispasmodic efficacy. Additionally, tissues were pretreated with a plant extract that made the Ca²⁺ dose-response curves shift to the right. This impact was comparable to that of common calcium channel blockers like verapamil. Additional fractionation work revealed that the n-hexane fraction is more effective than the ethyl acetate fraction. This research showed that *A. calamus* has antispasmodic properties⁴⁰.

Calendula officinalis L.: There are many purposes for which *C. officinalis* is utilized. *Calendulin*, *coumarin*, *loliolide*, and *carotenoids* are typical examples of the biological components found in these plants⁴¹. Burns, hemorrhoid hemorrhage, fever, cramping, and diabetic foot are just a few of the problems that *C. officinalis* is used to treat. It showed the ability to be hepatoprotective, nephroprotective, antiedematous, anti-inflammatory, and antioxidant⁴². Additionally, *C. officinalis* flowers have antispasmodic qualities. *C. officinalis*' aqueous-ethanolic extract was utilized to treat isolated gastrointestinal preparations for spasms. In the rabbit jejunum, the plant extract demonstrated dose-dependent (0.03-3.0 mg/mL) relaxing activity. Calcium channel blockage was used to mediate relaxation activity⁴³.

TABLE 1: SOME ANTISPASMODIC COMPOUNDS WITH MECHANISM OF ACTIONS

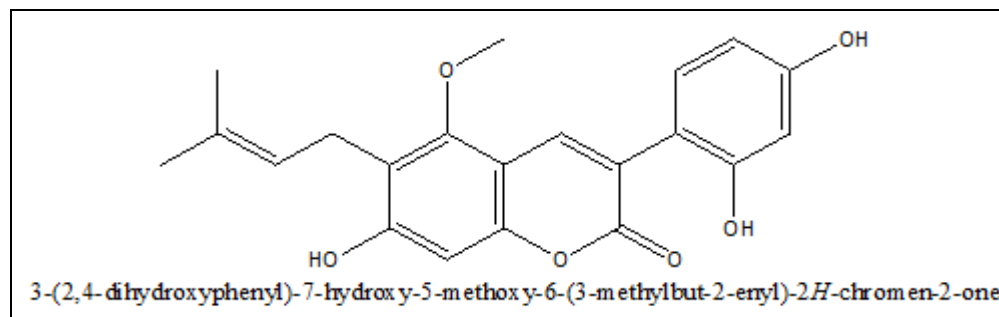
Antispasmodic plant	Compound name	Part used	Mechanism of Action	References
<i>Glycyrrhiza uralensis</i>	Glycycomarin	Root	Inhibitory action of acetylcholine and histamine-induced contractions	44
<i>Plectranthus barbatus</i>	Myrcene	Leaf	Acetylcholine inhibition	45
<i>Cynara scolymus</i>	Cynaropicrin	Leaf, flower	Acetylcholine inhibition	46
<i>Artemisia vulgaris</i>	Ezozlantonin	Leaf	Blockade of muscarinic receptors and calcium influx	47
<i>Thymus vulgaris</i>	Thymol	Whole plant	Effect on anticholinergics and serotonergic pathways	48
<i>Radix aucklandiae</i>	Costunolide	Rhizome	Inhibition of muscarinic receptors and calcium influx	49
<i>Allium elburzense</i>	Agapanthagenin	Bulb and flower	Decrease the activities of methanogenesis	50
<i>Allium cepa</i>	Tropeoside B1 and B2	Bulbs	Spasmolytic effect via calcium channels	51
<i>Tylophora hirsuta</i>	α -Amyrin acetate	Aerial parts	Calcium channel blockade	52
<i>Zingiber officinale</i>	Phellandrene	Rhizome	Antihistaminergic, antiserotonergic	53

<i>Moringa oleifera</i>	Niazinin	Seed	Inhibited acetylcholine-induced contractions	54
<i>Drosera rotundifolia</i>	Quercetin	Dried aerial parts	Affecting the allosteric binding site of the muscarinic M3 receptors inhibits neutrophil elastase	55
<i>Tamarindus indica</i>	Compesterol	fruits	Calcium channel blockade	56
<i>Anethum graveolens</i>	Anethin	Dill fruit	Potassium channel opening	50
<i>Matri cariarecutita L.</i>	Flavonoids	flower	Calcium channel blockade	57

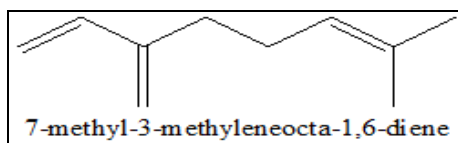
Chemistry of Active Ingredients:**Glycocoumarin:**

Coumarin derived

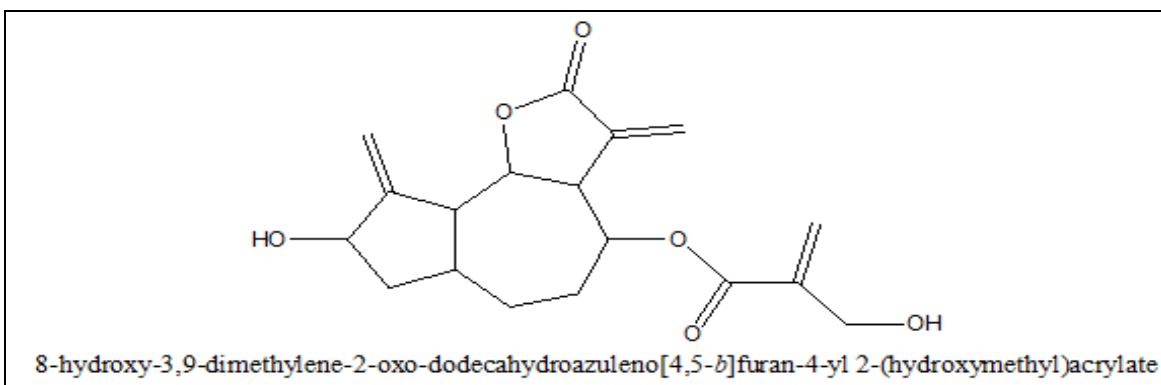
Glycocoumarin is substituted with hydroxyl group

at 7th position, a methoxy group at 5th position, a 2,4-dihydroxyphenyl group at 3rd position.

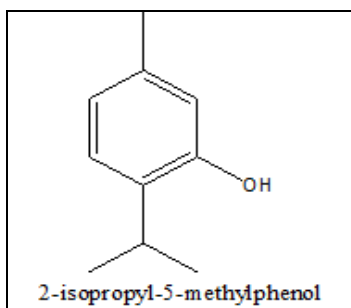
Myrcene: β -Myrcene, a monoterpene which is octa-1,6-diene substituted with methylene and methyl group at 3rd and 7th position.



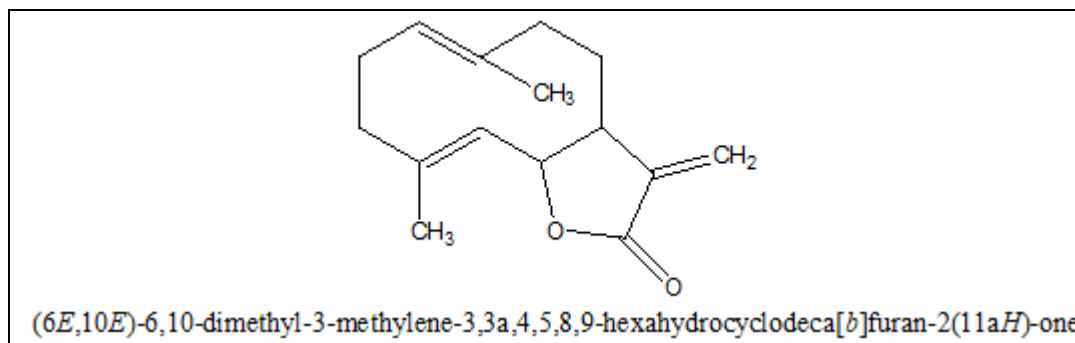
Cynaropicrin: Cynaropicrin is a tricyclic analog that contain two hydroxyl group on each side of molecule. Its γ -butyrolactone ring is responsible for most of the biological activity. The unsaturated carbonyl group on lactone ring involves Nucleophilic Michael addition.



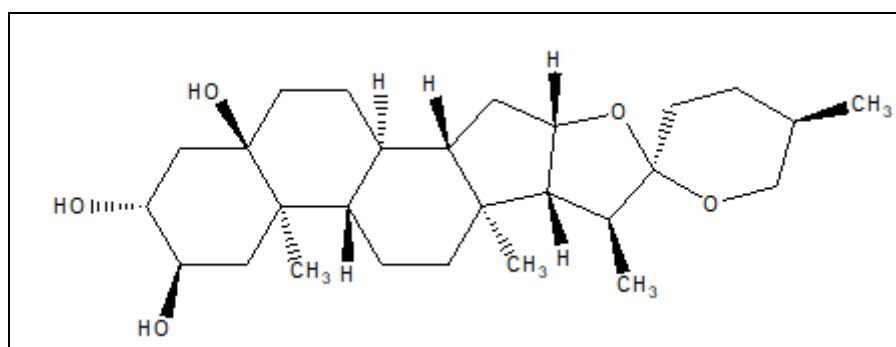
Thymol: It is a phenol which is obtain from cymene. It is a promising component for therapeutic activities. It consist of a methyl group in 5th position.



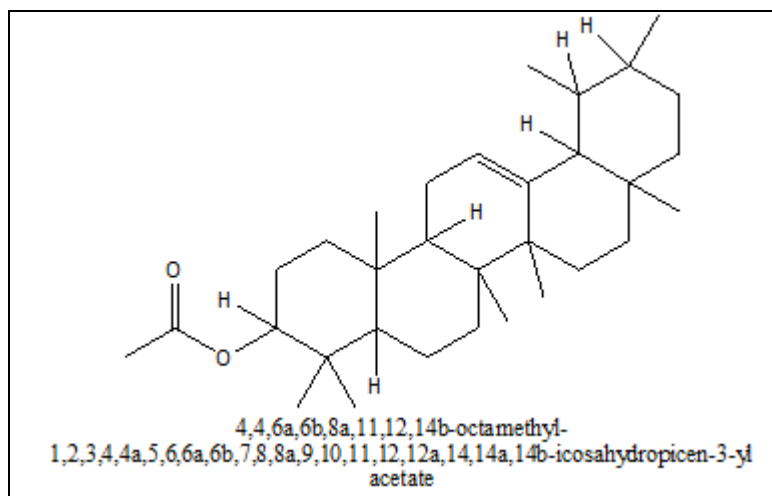
Costunoloid: The γ -butyrolactone structure of containing component which are essential for the Costunoloid undergo Michael reaction with SH- inhibitory activities.



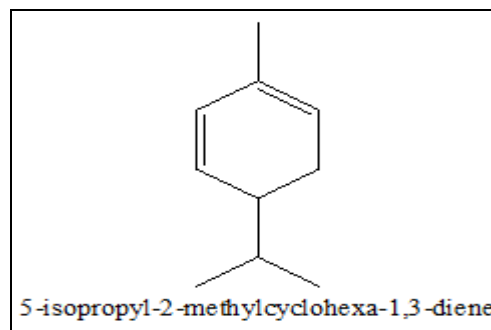
Agapanthagenin:



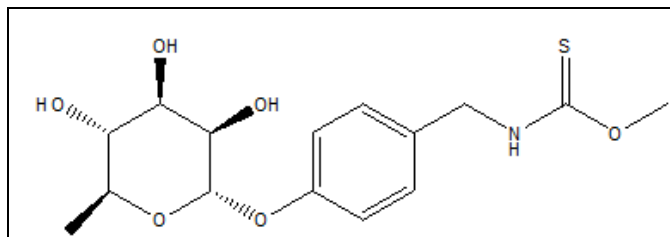
α - Amyrin Acetate:



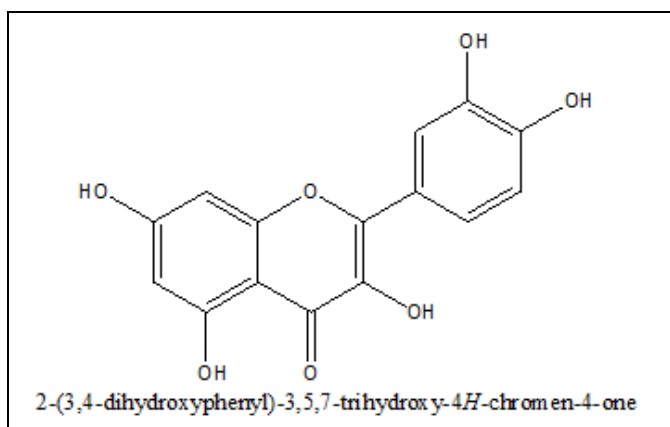
Phellandrene:



Niazinin: Niazinin is a thiocarbamate glycoside with various activities. It carries a methyl group in the ortho position in the phenyl ring.



Quercetin: Quercetin inhibits angiotensin-II induced by NADPH oxidase. It prevents endothelial dysfunction by intracellular redox process.



Present Overview: Antispasmodic therapeutic drugs are the treatments that may result in a better level of GIT muscle spasm relief and also reduce the liquid component of GIT to inhibit diarrhea. The activation of cholinergic/muscarinic, opioid, and histaminic receptors causes the spasm. Along with other body parts, the GIT also has these receptors. The M1, M3, and M5 cholinergic receptors are stimulated, which stimulates intracellular signaling and activates PKA and PKC. The calcium channel is stimulated by both of these kinase enzymes, which also increase intracellular calcium through increasing calcium inflow. The opening of calcium gates at ER and the release of calcium to the cytoplasm also result in an increase in intracellular calcium. The interaction between the elevated calcium level and the smooth muscle (SM) induces complete contraction, which also results in diarrhea. The primary working principle of antispasmodic experiments is this. The plant components or the extract/fraction in the medicinal plants mentioned above that have antispasmodic effects inhibited these receptors.

When these receptors are blocked, the amount of cAMP significantly decreases, and PKA/PKC is inhibited, which leads to a reduction in intracellular calcium. This decreased calcium level will cause the SM to relax because it is no longer adequate to constrict it. Antispasmodic effect or antidiarrheal effect are two terms used to describe this relaxing impact on SM.

In besides this, other writers have lately shown the antispasmodic potential of various plants. Regarding this, researchers from Algeria have reported on the inflammatory, antispasmodic, and healing activities of *Juglans regia* L. utilizing *in-vivo* models (58). The spasmolytic effects (spontaneous and precontracted tissues) of Digas colic drops (DCD-684), a polyherbal formulation of five distinct medicinal plants (*Carum carvi* L., *Foeniculum vulgare* Mill., *Mentha arvensis* L., *Mentha piperita* L., and *Zingiber officinale* Roscoe), were assessed. Both spontaneous (IC50: 0.75%) and KCl-induced contractions (IC50: 1.6%) were spasmolytically affected by DCD-684. Due to the inclusion of many bioactive substances, the DCD-684 displayed synergistic effects. Its postulated molecular mode of action is controlled by muscarinic and/or nicotinic receptors, serotonergic histaminergic, coupled with calcium channel blocking mechanisms⁵⁹. Papaverine (derived from *Papaver somniferum*) and its synergistic benefits with the well-known medication Imatinib were discussed in another research by *Parcha et al.* against Chronic Myeloid Leukaemia⁶⁰.

CONCLUSION: Based on the information collected, it may be stated that traditional natural remedies are a reliable, cost-effective method of treating spasmodic pain. Numerous plant species have been found as a result of this analysis that reduce spasmodic pain with little toxicity or negative effects. The use of herbal remedies for a number of diseases is supported by current study results. In light of this, additional research is being done to determine the possible antispasmodic effects of various plant species, which merit further attention in terms of *in vivo* and clinical trial investigations. The thorough literature review of medicinal plants may be a rich source of antispasmodic chemicals, opening up new study opportunities for academics and researchers in this

subject. Therefore, more pharmacokinetic and pharmacodynamic studies should be conducted together with clinical trials to confirm the effectiveness and outline the safety profile of conventional medications used to treat spasmodic diseases.

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