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Review Article

A Review on Herbal Antispasmodics

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ABSTRACT

Numerous medicinal plants are utilized for the treatment of different type of disorders and diseases. Most children and adolescent suffer from muscle cramps as a result of many disease conditions. The antispasmodic effect of drugs is used for the symptomatic treatment of cramping and discomfort affecting smooth muscles in a variety of clinical situations. Main aim of this review is to emphasis the therapeutic potential of plants possessing antispasmodic effects. These medicinal plants and their herbal products are passed down through generations due to their wide range of nutritional and therapeutical benefits including menstrual cycle disorders, gastrointestinal diseases, epilepsy. Additionally, the study also revealed that the active compounds of these plants possess significant spasmolytic effect. This review underscores the importance of medicinal plants as potential sources of safe and effective antispasmodic agents.

INTRODUCTION

Anti-spasmodic drugs are agents which have the ability to relieve muscle spasm [(1)]. Most commonly, gastrointestinal disorders are reported among children in most of the globe. Gastrointestinal disorders can lead to decreased life quality and increased risk of anxiety and depression [(2)]. In the ayurvedic system, the ancient Indian medicine system, emphasises using natural remedies derived from plants to promote health and well-being [(3)].

REVIEW OF HERBAL DRUGS

Ammodacus leucotrichus

Ammodaucus leucotrichus belonging to the family Cupressaceae which is commonly known as cade juniper. It is used to eradicate stomach ache, fever, intestinal worms, spasms, and constipation. Perillaldehyde and limonene are the major chemical constituents along with minor components like perilla alcohol, flavonoids, phenolic acids, lignans and terpenoids. The *in-*

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vitro method on isolated smooth muscle of guinea pig ileum was used to evaluate antispasmodic activity of *Ammodaucus leucotrichus.*

Mechanism of action:

- Inhibition of calcium channel: The extract of *Ammodaucus leucotrichus* caused a rightward shift in $CaCl_2$ response curves which resembles the effect of classic L-type calcium channel blockers.

Clinical applications:

- Antidiarrheal: The methanol extract of *Ammodacus leucotrichus* is used to treat diarrhoea
- Management of intestinal spasms: It is used to treat intestinal spasm [4]

Juniperus oxycedrus

Juniperus oxycedrus is an evergreen plant belonging to the family Cupressaceae and it is also known as cade juniper, prickly juniper. It provides various therapeutic activities like analgesic, antibacterial, and anti-cancer activity. The active chemical constituents include manoyl oxide, caryophyllene oxide, myrcene and alpha-pinene and germacrene D. *In-vivo* and *In-vitro* methods on rodents were used for evaluating antispasmodic activity.

Mechanism of action:

- Calcium channel blocking: It acts as noncompetitive blocker for calcium channels
- Potassium channel activation: The plant's extract opens the potassium channel which leads to hyperpolarization and reduces the excitation of smooth muscle.
- Muscarinic receptor antagonist: It blocks the muscle contractions induced by carbachol.

Clinical applications:

- Gastrointestinal spasm management: *Juniperus oxycedrus* extracts reduce antispasmodic effects. They inhibit contractions of smooth muscle by regulating of calcium channels.
- Anti-diarrheal: *Juniperus oxycedrus* reduces the gastrointestinal motility. It is due to the modulation of smooth muscle contractions [5].

Alstonia boonei

Alstonia boonei belonging to the family Apocynaceae which is also known as Cheese wood is a tropical tree from Africa. They were known for producing antispasmodic action, analgesic effects and anti-inflammatory action. Its active chemical constituents are boonein, beta-Amyrin. Antispasmodic activity was evaluated by *Ex-vivo* assay on isolated rat ileum.

Mechanism of action:

- Muscarinic receptor blockade: The *Alstonia boonei* extract was able to block the muscarinic receptor which reduces the smooth muscle spasm.
- Inhibition of calcium channels: *Alstonia boonei* may block the potassium chloride induced contractions by blocking the calcium channel.

Clinical applications:

- Treatment for diarrhoea: *Alstonia boonei* reduces the intestinal motility, which reduces the contribution to diarrhoea.
- Treatment of gastrointestinal spasms: *Alstonia boonei* is used to treat irritable bowel syndrome and abdominal cramps [6].

Atropa belladonna

Atropa belladonna belonging to the family Solanaceae is also known as deadly nightshade. It inhibits muscarinic receptors, relaxing smooth muscle. It contains atropine, scopolamine, and hyoscyamine as the active constituents. Scopolamine exhibits a more potent antispasmodic effect than atropine.

Mechanism of action:

- Competitive antagonism: Atropine and its analogues usually compete with Ach at muscarinic receptors without activating them. It inhibits the activity of the parasympathetic nervous system, which typically governs the body's rest and digest processes.

Clinical applications:

- **Ophthalmology:** Mydriasis and cycloplegia: Atropine, extracted from *Atropa belladona*, is used in the eye drops to dilate pupils and paralyze the cliliary muscle. It's critical for refractive assessments, uveitis management, amblyopic treatment, and preventing posterior synechiae.
- **Myopia control:** Low dose atropine has been shown to slow myopia progression in children [(7)]

Foeniculm vulgarae mil

Foeniculum vulgare Mill belonging to the family Apiaceae also known as Saunf is known for its culinary and medicinal uses, with its seeds and aerial parts utilized in traditional remedies and flavoring. The chemical constituents such as anethole, fenchone, estragol, flavonoids, phenolic compounds, fatty acids, vitamins are the active constituents responsible for anti-spasmodic actions. *In-vitro* assay on guinea pig ileum was conducted to evaluate the antispasmodic activity.

Mechanism of action:

- Potassium channel activation: Potassium channel activation *in vitro* work on guinea pig trachea tissue showed the fennel's ethanol extract and essential oil did not block the calcium channel but promotes relaxation of smooth muscle by activating potassium channels, a mechanism which is similar to that of bronchodilators.
- Muscarinic contraction inhibitor: It's oil reduces the contractions made by histamine.

Clinical applications:

- Reduced gastrointestinal transit: The formulation reduces the gastrointestinal movements [(8)].

Lavandula angustifolia

Lavandula angustifolia belonging to the family Lamiaceae also known as Lavender is prized for its aromatic leaves, flowers, and essential oil, which are used in various applications, including perfumery, cosmetics, and medicine. The active constituents responsible for its antispasmodic actions are linalool, linalyl acetate, cineole, camphor, borneol.

Mechanism of action:

- cAMP modulation: Chemical constituents linalool usually increase cAMP in the muscles which causes the relaxation in the conjunctiva and ileum.
- Acetylcholine induced action: cineole reduces acetylcholine muscle contraction which produces spasmolytic activity.

Clinical applications:

- Ocular spasm: It is applied in some of the herbal formulations for the treatment of conjunctival irritation and spasm.

- General stress induced muscle tension: Helps to suppress tension headache or muscle tightness induced by stress by CNS calming and muscle relaxation [9].

Matricaria chamomilla

Matricaria chamomilla belonging to the family Asteraceae commonly known as German chamomile often used for its medicinal properties. It is native to Europe and Asia and is now found globally. Chamomile has been traditionally used to treat 5 ailments, including gastrointestinal issues, colds, liver problems, and skin conditions. Volatile oils, flavonoid and phenolic acids are the chemical constituents responsible for the action. The antispasmodic activity was evaluated by *In-vitro* organ bath assay with isolated gut tissue.

Mechanism of action:

- Potassium channel activation: opening of voltage-dependent and ATP sensitive potassium channels in smooth muscle of the gut which result in the hyperpolarization leads to muscle relaxation which then causes reduced spasms.
- Weak Calcium channel inhibition: At higher concentrations, Chamomile shifts calcium dose response curves to the right side indicating the modest calcium channel antagonism which will contribute the anti-spasmodic effect.

Clinical applications:

- Mild sedative effects: Flavonoids like apigenin contribute the calming effects, easing digestion related nervous tension.
- Anti-diarrheal: It reduces watery diarrhea and reduces the gut secretions [10].

Mentha piperita

Mentha piperita belonging to the family Lamiaceae also known as peppermint is used as an effective antispasmodic for the treatment of gastrointestinal disorders, respiratory disorders, neurological and pain-related conditions. Menthol is the main active constituent that produces the antispasmodic activity. *Ex-vivo* organ bath motility assay on guinea pig gut tissue was done to determine the antispasmodic activity.

Mechanism of action:

- Calcium channel modulation: Menthol interacts with smooth muscle calcium channel reducing calcium influx into the cell, thereby promoting relaxation of intestinal muscles.
- Direct antispasmodic effect: The compound visibly relaxes smooth muscle, leading to antispasmodic effect.

Clinical applications:

- GI motility disorder management: provide muscle relaxation in case of abdominal cramps, bloating and colic. Reduces pathological motility in ileum, colon and stomach making it useful for functional GI disorders.
- Supportive role in dyspepsia: By compiling menthol with fennel and other herbs, the formulation offers holistic symptom relief in indigestion and functional dyspepsia [11].

Calotropis Gigantea

Calotropis gigantea belonging to the family Apocynaceae also known as Crown flower used as an antispasmodic in the treatment of diarrhea and gastrointestinal disorders. Cardenolide glycoside, triterpenoids, steroids, flavonoids, phenolics, alcohols are the active constituents. Phytochemical and pharmacological review were conducted to evaluate its antispasmodic activity.

Mechanism of action:

- Sodium/Potassium ATPase inhibition: Calotropin inhibits Na^+/K^+-ATPase which leads an increase in intracellular calcium concentration which in turn increase the contractility of heart.

Clinical applications

- Anticancer action: It helps to destroy tumor cells by apoptosis.
- Analgesic: The plant's extract has an analgesic effect similar to that of NSAID's especially for joint and muscle pain.
- Antidiarrheal activity: Reduces the gastrointestinal motility especially for treating acute diarrhea [12].

Gentiana lutea

Gentiana lutea belonging to the family Gentianaceae also known as yellow gentian is used as an antispasmodic drug for the treatment of gastrointestinal disorders, abdominal cramps, irritable bowel syndrome, flatulence and colic, indigestion, and hypermotility disorders. Secoiridoids, xanthones, and flavonoids are the main active constituents responsible for the antispasmodic activity. The evaluation of antispasmodic activity was done by *Ex-vivo* organ bath assay on rat ileum.

Mechanism of action

- Inhibition of calcium channels: The extract blocks voltage dependent calcium channels, reducing calcium influx into smooth muscle cells. This lowers intracellular calcium preventing muscle contraction.
- Activation of potassium channels: opens specific potassium, ATP sensitive and voltage gated channels causing hyperpolarization of smooth muscle membrane, making it less excitable.
- Suppressions of Neurotransmitter induced contractions: The extract reduces spasm triggered by acetylcholine and histamine, blocking muscarinic and histamine receptor pathway indirectly.

Clinical applications

- Treatment of gastrointestinal spasms: The extracts ability to relax smooth muscle supports its use in relieving spasmodic abdominal pain, bloating, and cramping in conditions like irritable bowel syndrome, functional dyspepsia, intestinal colic.
- Adjunct in digestive disorders: Traditionally used as a bitter tonic, *Gentiana lutea* also stimulates digestion. It stimulates appetite while calming spasm makes it helpful in indigestion with motility issues [13].

Antispasmodic plant	Name of the compound	Part of the plant used	Mechanism of action	References
Glycyrrhiza uralensis	Glycocoumarin	Root	Inhibitory actions of acetylcholines and histamine induced contractions	(14)
Plectranthus barbatus	Myrcene	Leaf	Acetylcholine inhibition	(15)
Thymus vulgaris	Ezolantotonin	Leaf	Blockade of muscarinic receptors and calcium influx	(16)
Allium elburzense	Agapanthagenin	Rhizome	Inhibition of muscarinic receptors and calcium influx	(17)
Allium cepa	Tropeoside B1 and B2	Bulb and flowers	Decrease the activities of methanogenesis	(18)

Tylophora hirsuta	Amyrinacetate	Bulbs	Spasmolytic effects via calcium channels	(19)
Zingiber officinale	Phellandrine	Aerial parts	Calcium channel blockade	(20)
Moringa oleifera	Niazinin	Rhizome	Antihistaminergic, antiserotogenic	(21)
Drosera rotundifera	Quercetin	Seed	Calcium channel blockade	(22)
Tamarindus indica	Compestrol	Dried aerial parts	Pottasium channel blockade	(23)
Anethum graveolens	Anthenin	Dill fruit	Acetylcholine inhibitor	(24)
Matri cariarecutita L.	flavonoids	Flower	Calcium channel blockade	(25)

CONCLUSION

It might be concluded based on the obtained information that the spasmodic pain can be treated by traditional natural medicines, which are effective, safe, and economical. Unlike the synthetic antispasmodics, Herbal antispasmodics usually considered having less chance of having side effects, adverse drug reactions. Different methodologies have been used for the evaluation of antispasmodics. Under this review, many plant species have been identified that reduce spasmodic pain with low toxicity and side effects. Thus, herbal antispasmodic agents emerge as effective alternatives with reduced risk of toxicity and adverse effects.

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