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Medicinal plant affected respiratory, gastrointestinal, vascular and uterine smooth muscle contractility

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Abstract

In the current review, PubMed, Web Science, Science Direct, and Scopus were searched to investigate the medicinal plants which contracted or relaxed the respiratory, gastrointestinal, vascular and uterine smooth muscles with emphasis on their mode of action.

Keywords: Respiratory; Gastrointestinal; Vascular; Uterine; Smooth Muscles; Contraction; Relaxation

1. Introduction

In a healthy body, the process of contraction of smooth muscle cells is regulated mainly by activation of receptors and mechanical stimulation (stretching) of contractile proteins. A change in the membrane potential, caused by the release of an action potential or by activation of stretch-dependent ion channels in the plasma membrane, can lead to contraction. Smooth muscle relaxation occurs either as a result of removal of the contractile stimulus or by the direct action of a substance that stimulates inhibition of the contractile mechanism. Regardless, the process of relaxation requires a decreased intracellular Ca^{2+} concentration and increased MLC phosphatase activity [1-2]. Medicinal plants induced contraction or relaxation of smooth muscles by many mechanisms included interference with neurotransmitters, neuro-mediators, second messengers, ionic channels and other mechanisms [3-8]. The current review focused on medicinal plants affected the function of vascular, respiratory, uterine and gastrointestinal smooth muscles.

Table 1 Medicinal plant affected respiratory smooth muscle contractility

Medicinal plant	Extract or compounds	Model	Action	Ref
Allium cepa	Five alk(en)yl sulfinothioic acid alk(en)yl-esters isolated from onion	Bronchial tissue of guinea-pigs	Five alk(en)ylsulfinothioic acid alk(en)yl-esters isolated from onions inhibited allergen- and PAF-induced bronchial obstruction of guinea-pigs.	9
	Isothiocyanate compounds isolated from onion	Bronchial obstruction induced by inhalation of ovalbumin	Benzyl-isothiocyanate (BITC) inhibited BO in a dose-dependent fashion: 150 mg/kg: 89%; 75 mg/kg: 76%; 30 mg/kg: 66%; 15 mg/kg: 49%. Ethyl-isothiocyanate and allyl-isothiocyanate showed similar effects, while, p-hydoxy-benzyl-isothiocyanate, was ineffective.	10-11

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		in guinea-pigs		
	Extract obtained by maceration	Effects on cytokine and on smooth muscle contraction *in vitro* and its therapeutic potential in a murine model of asthma	*Allium cepa* extract caused relaxation of tracheal rings, and a reduction in total number of cells in broncho-alveolar lavage and eosinophil peroxidase in lungs.	12-13
Allium sativum	Aqueous bulb extract containing 0.06%-0.10% of allicin	Isolated smooth muscle of trachea of rats	It induced a dose-dependent relaxation with recorded EC_{50} values of 71.87 ± 5.90 μg/ml. Pre-treatments with mepyramine (10^{-7} M), methysergide (10^{-7} M), caffeine (10^{-6} M), theophylline (10^{-6} M), nifedipine (10^{-6} M), and dipyridamole (10^{-6} M) did not alter *Allium sativum* bulb aqueous extract Concentration-response curves were significantly shifted toward right in the presence of aspirin (3.10^{-3} M), indomethacin (10^{-6} M), prazosin (10^{-6} M), and propranolol (10^{-7} M).	14
Ammi visnaga	Khella raw fruit	Clinical	Khella's antispasmodic properties are also useful to treat asthma attacks. During the 1950's, research into khella's usefulness as an asthma treatment led to the creation of many asthma medications containing khellin and visnagin	15-16
Andrachne aspera	Alcoholic extract of the aerial parts	Tracheal muscle of cat	It showed significant spasmolytic activity on tracheal muscle of cat.	17-19
Anthemis nobelis	Chamomile was boiled and immediately used by inhalation for 5-10 minutes using vapor machine	Clinical	In an open clinical study carried out on 54 patients with chronic bronchial asthma, it showed anti-asthmatic effects, it caused significant elevation in the values of forced expiratory volume in first second (FEV_1%) and forced volume capacity (FVC) with marked reduction in asthmatic attacks.	20-21
Bacopa monnieri	Ethanol extract	Guinea -pig trachea in calcium free high K^+-MOPS-PSS	The plant extract (500 and 700 µg/ml) significantly ($P < 0.05$) depressed and shifted the calcium concentration-response curves (1×10^{-3}- 1×10^{-1} M) to rightward similar to that of nifedipine.	22
	Methanolic fraction	Mast cell stabilization	It exhibited potent activity comparable to disodium cromoglycate, a known mast cell stabiliser.	23-24
Calotropis procera	Aqueous extract	Tracheal smooth muscle chain of Guinea-pig	50, 100 and 200 µg/ml of the extract showed a dose-dependent direct relaxant activity.	25-26

Carum carvi	Aqueous extract (AE), macerated extract (ME) and essential oil (EO)	Isolated tracheal chains of guinea pigs	The broncho-dilatory effects were studied by examining the relaxant effects on pre-contracted by 10 /µM methacholine (M) of the isolated tracheal chains of guinea pigs. The broncho-dilatory effect of AE, ME, and EO was lower than that of theophylline (p<0.00l), but it was significantly higher than the effect of saline (p<0.05 for AE, p<0.01 for ME, and p<0.005 for EO). The broncho-dilatory effect was mainly due to the non-competitive antagonistic property at muscarinic receptors. The β- stimulatory effect and/or anti-histaminic effect of EO might be contributed to its non-competitive property.	27-28
Casuarina equisetifolia	of methanolic extracts of wood, bark, fruit and leaf	Tracheal chain	The extracts of wood and bark inhibited the histamine induced contraction of trachea (10-80 mcg/ml) in dose dependent pattern (P<0.05) while leaf and fruit extracts were without any effects. The successive chloroform extract demonstrated more activity (63.30 ± 10.33) as compare to petroleum ether (87.5 ± 13.24) and methanolic extract (166.66 ± 23.32) of wood (P<0.05). The chronic treatment of methanolic wood extract (100 mg/kg, ip) significantly reduced the clonidine induced catalepsy at 60 and 120 minutes (P<0.05) and mast cell degranulation (72.50±8.37) against standard, disodium cromoglycate, (85.19 ± 4.30) (P<0.001)	29-30
Cordia myxa	Alcoholic extract	Sheep trachea.	*Cordia myxa* extract inhibited contraction in both epithelium-intact and denuded sheep trachea rings induced by acetylcholine. The scale of relaxation with *Cordia myxa* extract was dose dependent and slightly more potentin epithelium denuded rings than epithelium-intact preparations. L-NAME (10 nM-100 uM) but not DNAME completely inhibited the relaxant effect in a concentration dependent manner. *Cordia myxa* extract -induced relaxation was inhibited by methylene blue (1 -100 uM), and verapamil (100 nM), and removal of extracellular Ca^{2+}. In contrast, *Cordia myxa* extract - induced relaxation was potentiated by L-NOARG treatment.	31-32
Crocus sativus	Hydroethanolic extract of stigma and safranal	Guinea pig tracheal chains and ovalbumin-sensitized guinea pigs	It caused relaxant, inhibitory effect on histamine (H1) and muscarinic receptors, and stimulatory effect on β-drenoceptor on guinea pig tracheal chains. The results showed a preventive effect of the extract and its constituent safranal on total and differential count of WBC in blood of sensitized guinea pigs.	33-34
Dolichos lablab	Alcoholic fraction	Respiratory smooth muscles	Sixty seven percent inhibition of spasm in respiratory smooth muscles were observed of *Dolichos lablab* alcoholic fraction at 100 mg/kg body weight	35-36
Ephedra species	Ephedrine	Tracheae of cats, dogs, rabbits, guinea-pigs, and rats. Clinical	The smooth muscle of the bronchial tree was relaxed by ephedrine. Compared with epinephrine, the action of ephedrine was slow in onset, complete an hour or more after administration. Ephedrine also prevented histamine-induced broncho-constriction in patients with asthma.	37-39
Hibiscus sabdariffa	Aqueous extract	Guinea -pig tracheal	Inhibited the tone of guinea-pig tracheal chain and rat diaphragm).	40-41

		chain and rat diaphragm		
Hyoscyamus niger	The crude extract of the seeds	Guinea -pig trachea	It produced antispasmodic effect mediated through a combination of anticholinergic and Ca^{2+} antagonist mechanisms.	42-43
Leontice leontopetalum	Low conc. of petaline chloride, a quaternary alkaloid from *Leontice leontopetalum*	Isolated trachea	Caused no effect on the trachea. Larger concentrations (up to 3 mg/ml) caused nonsustained large contractions of the trachea. The contractile effects were not inhibited by atropine	44-45
Lepidium sativum	Crude extract	Guinea - pig tracheal ring strips	Inhibited carbachol (1 μM) and K+ (80mM) induced contractions in Guinea pig tracheal ring strips, in a pattern similar to that of dicyclomine. The crude extract at 0.03 mg/ml produced a rightward parallel shift of carbachol curves, followed by nonparallel shift at higher concentration (0.1 mg/ml), suppressing maximum response, similar to that caused by dicyclomine.	46-47
Lythrum salicaria	Polysaccharide - polyphenolic conjugate isolated from flowering parts of*Lythrum salicaria*	Airways smooth muscle reactivity in guinea pigs	Measurements of specific airway resistance revealed dose-dependent broncho-dilatory activity	48-49
Melissa officinalis	The leaves oil	Guinea - pig tracheal	possessed relaxant effects on the guinea pig tracheal.	50-51
Mirabilis jalapa	The ethanol: acetone (1:1) extract(0.5 ml of 100 mg/ml)	Guinea - pig tracheal chain	Inhibited histamine-induced guinea pig tracheal chain contractions non-competitively.	52-53
Morus nigra	Phenolic compounds	Rat tracheal smooth muscles	Phenolic compounds (kuwanon U, moracin O and albanol B) showed strong antispasmodic	54
Myrtus communis	Crude methanol extract	Rabbit tracheal preparations	The crude methanol extract exhibited relaxant effect on CCh- and K^+ (80 mM)-induced contractions in isolated rabbit tracheal preparations.	55
Nigella sativa	Thymoquinone	Guinea- pig tracheal smooth muscle	Thymoquinone caused a concentration-dependent decrease in the tension of the tracheal smooth muscle pre-contracted by carbachol, when investigated in Guinea pig isolated tracheal zig-zag preparation. It totally abolished the pressor effects of histamine and serotonin on the Guinea pig isolated tracheal smooth muscles. These effects were suggested to be mediated, at least in part, by inhibition of lipoxygenase products of arachidonic acid metabolism and possibly by non-selective blocking of the histamine and serotonin receptors.	56

Table 2 Medicinal plant affected gastrointestinal smooth muscle contractility

Medicinal plant	Extract or compounds	Model	Action	Ref
Allium sativum	Application (4 g/ml)	Rabbit duodenum	An increase of the spontaneous contraction of rabbit-duodenum was established by garlic solution. Blockade the M_3 muscarinic receptors of the smooth muscle by atropine sustained normal contraction.	57
Ammi visnaga	Boiled distilled water seeds extract	Rabbit jejunum	It caused reduction of intestinal contraction. Neostigmine and pilocarpine effect was inhibited by the administration of *Ammi visnaga*.	58
Andrachne aspera	Alcoholic extract of the aerial parts	Guinea -pig ileum and rat ileum	It showed spasmolytic activity and and antihistaminic activity on guinea pig ileum.	17-19
Anthemis nobelis	Crude herbal extract	Guinea-pig ileum	The crude herbal extract induced an immediate, moderate, and transient contraction of guinea pig ileum via the activation of cholinergic neurons of the gut wall.	59
Arundo donax	A defatted ethanolic extract of the rhizomes	Rats	It produced antispasmodic effects against histamine, serotonine and acetylecholine induced spasms.	60-61
Asparagus officinalis	Aqueous extract	Smooth muscle of rabbit jejunum	It caused relaxation of spontaneous contractions of isolated smooth muscle of rabbit jejunum.	62-63
Calotropis procera	Ethanol , n-butanol, and ethyl acetate extracts	Duodenum and ileum smooth muscles in rats	They induced stimulatory effect which abolished by atropine, indicated that the stimulatory effect on smooth muscle was mediated by cholinergic effect.	64-66
	Dry latex	Smooth muscles of gastro-intestinal tract in rats and rabbits	50-1000 mg/kg of dry latex produced a dose-dependent decrease in intestinal transit along with a decrease in intestinal content. At lower doses dry latex produced dose-dependent gastro-intestinal smooth muscles in vitro (rabbit ileum and fundus of rat stomach) that was followed by desensitization at higher doses.	67
	Latex alone and with loperamide and atropine	On intestinal transit in rats using charcoal meal test	Latex of *Calotropis procera* inhibited intestinal motility and its action was potentiated by atropine and loperamide.	68
Capsella bursa-pastoris	Several extracts	Small intestine in the guinea-pig	The plant induced stimulatory action unaffected by atropine and diphenhydramine, but were inhibited by papaverine.	69-70
	Extract of dried or green plant	Guinea pig small intestine	The extract of dried or green plant causes strong contraction of the small intestine of guinea pigs. A quarternary ammonium salt has been isolated from the herb which is reported to be responsible for this activity.	71
Cassia occidentalis	Soaking seeds extract	*In vivo* and in vitro, intestinal and lung	The maximal contractile responses of the treated birds decreased significantly compared to those of the control group. The decrease was also	72-73

		parenchimal strips of chickens	directly related to the length of treatment. The day 5 group showed the maximum decrease. The *in vitro* study suggested involvement of smooth muscles as a primary site for the toxicosis caused by *Cassia occidentalis*. The decrease in maximal response of lung parenchymal strip suggested the existence of an active principle(s) in the extract which caused the effect by systemic absorption.	
Casuarina equisetifolia	Bark extract	Isolated ileum	The bark extract reduced contractions in isolated ileum induced by spasmogens like ACh, Histamine, KCl and BaCl and potentiated the effect of Nifedipine suggesting an antimuscarinic, antihistaminic and a calcium channel blocking action.	74-75
C*henopodium album*	The plant was extracted in ethanol and fractionated in ethyl acetate, chloroform, *n*-butanol and water.	Intestinal smooth muscles of rabbit	The crude extract exhibited a dose-dependent increase in relaxation of smooth muscles, starting from 5 mg/ml and maximum effect was found at 20 mg/ml (92.86%). The ethyl acetate and chloroform fractions of C*henopodium album* exhibited relaxation of the intestinal muscles (43.48 and 51.52%, respectively); whereas, *n*-butanol fraction of C*henopodium album* produced strong relaxant effect (91.18%).	76-77
Clerodendrum inerme	Methanolic extract	Rabbit jejunum and rat uterus	The extract produced the normal rhythmic contraction of rabbit jejunum, which reversed by prior addition of cyproheptadine. Methanolic extract also produced a stimulant activity on rat uterus which was blocked by cyproheptadin.	78-79
Crocus sativus	Petals ' aqueous extract	Guinea -pig ileum	The isolated guinea-pig ileum evoked contractions were decreased by aqueous and ethanol extracts of *Crocus sativus* petals.	80
Dodonaea viscose	Compounds isolated from the chloroform-methanol (1:1) extract (sakuranetin , 6-hydroxy kaempferyl 3,7-dimethyl ether, hautrivaic acid, and ent-15, 16-epoxy-9 alpha H-labda-13(16)14-diene-3 beta, 8 alpha-diol)	Guinea -pig ileum	All the isolated compounds elicited a concentration-dependent inhibition of the spontaneous and electrically-induced contractions of guinea-pig ileum. Sakuranetin and the ent-labdane inhibited ileum contractions evoked by acetylcholine, histamine, and barium chloride.	81-82
Erodium cicutarium	Several organic extracts	Guinea-pig ileum	Hexane extract, increased the tone of the guinea pig ileum preparation and reduced the strength of the contractions following field stimulation.	83-86
Equisetum arvense	Alcoholic extract	Guinea -pig ileum	The extract antagonized the effect of acetylcholine on the isolated guinea-pig ileum preparation.	87

Fumaria parviflora	Aqueous - methanol extract	Jejunum, ileum and tracheal preparations of rat, guinea-pig and rabbit	The aqueous-methanol extract predominately more potent against CCh than isotonic high K^+ solutions-induced contractions, similar to dicyclomine, suggesting the presence of anticholinergic and calcium channel blocking [CCB] activities, which were confirmed when the extract shifted the CCh and Ca^{2+} concentration-response curves in rat ileum and trachea, towards right. Among intestinal preparations from various species, both anticholinergic and CCB effects of the aqueous-methanol extract were exhibited at lower concentrations in rat than the other species. In tracheal preparations, the extract was the most potent in its CCB effect in rabbit.	88-89
Glycyrrhiza glabra	The hydro-alcoholic extract	Rat colon	The hydro-alcoholic extract of licorice had modifying effect on colon motility via synergist effect with beta adrenergic receptors and independent of the alpha adrenergic receptors.	90-91
	Isoliquiritigenin isolated from an aqueous extract of licorice	Several isolated tissues	It was a potent relaxant, inhibited the contraction induced by various types of stimulants, such as CCh, KCl, and BaCl2 with IC_{50} values of 4.96±1.97 microM, 4.03±1.34 microM and 3.70±0.58 microM	92-93
	Alcoholic extract of licorice rhizome	Rat duodenum pieces	Alcoholic extract of licorice rhizome decreases bowel motility. The contraction force exerted on the isolated duodenum pieces by acetylcholine was remarkably reduced in the presence of licorice rhizome extract compared to that of the control group ($P<0.05$).However, this response in the presence of atropine, propranolol and N-w-nitro- L arginine methyl ester (L-NAME) was not changed significantly.	94-95
Hibiscus sabdariffa	Methanol extracts	*In vivo* in rats and in vitro, rat ileal strip	a significant ($p < 0.01$) dose dependent relaxant effect (IC_{50} = 350 μM) on rat ileal strip comparable to the effect shown by nifedipin and papaverine. The extract when administered ip., it also significantly ($p < 0.05–0.01$) reduced the intestinal transit (13-35%) in rats (IC_{50} = 250 μM)	96
Juniperus oxycedrus	Methanol and dichloromethanol extracts of the leaves and stems	Different GIT tissues of rats and guinea-pigs	Extracts inhibited the concentration curve response to histamine, serotonin and acetylcholine induced contractions.	97-98
Hyoscyamus niger	The crude extract	Rabbit jejunum and guinea-pig ileum	It produced antispasmodic effect mediated through a combination of anticholinergic and Ca^{2+} antagonist mechanisms.	42-43
Lantana camara	Methanolic leaves extract	Rat ileum	Extract showed antispasmodic action on excised rat ileum. When acetylcholine was given in presence of methanolic leaves extract of *Lantana camara*, extract caused marked decrease in contraction of ileum, indicating blocking cholinergic receptors.	99-100

	Lantana camara leaf powder, *Lantana camara* methanolic extract,	Charcoal and castor oil models in mice	When the extracts at 125 and 250 mg/kg doses were administered ip, it caused significant reduction in fecal output compared with castor oil treated mice. At higher doses (500 and 1000 mg/kg), the fecal output was almost completely stopped.	101
Leontice leontopetalum	Low concentrations of petaline chloride, a quaternary alkaloid from *Leontice leontopetalum*	Isolated iliem	Caused contraction of the ileum, and no effect on the trachea. Larger concentrations (up to 3 mg/ml) increased the amplitude of the phasic contractions of the ileum. The contractile effects were not inhibited by atropine.	102
	Oblongine chloride, a quaternary alkaloid from *Leontice leontopetalum*	Guinea -pig isolated ileal longitudinal segments	Caused concentration-dependent relaxation of guinea-pig isolated ileal longitudinal segments, the effect was not blocked by propranolol (10-6 M) alone or in combination with prazosin (3×10^{-8} M), or by indomethacin (10^{-6} M), but was reduced by desensitization of the preparation by prior exposure to a combination of propranolol and yohimbine	103
Lepidium sativum	Aqueous methanolic extract of the seeds	Isolated gut preparations of mouse rabbits and guinea-pig: jejunum and ileum	caused a concentration dependent stimulatory effects both in jejunum and ileum, which was blocked by atropine. In rabbit jejunum, the stimulant effect of aqueous- methanolic extract remained unchanged in the presence of atropine, pyrilamine or SB203186, while in rabbit ileum, the stimulatory effect was partially blocked by atropine.	104
	Seed extract	Isolatedrat ileum	the extract (0.01-5 mg/ml) reversed carbachol (1 μM) and K+ (80 mM)- inducedcontractions with higher potency against carbachol.	105
	Crude extract	Isolated ileum and jejunum of many animals	crude extract completely inhibited carbachol, low K^+(25 mM) and high K^+(80 mM)-induced contractions, while in Guinea-pig tissues, crude extract caused complete inhibition of only carbachol induced contraction. In rabbit tissues, crude extract completely inhibited carbachol and low K^+ -induced contractions sensitive to K^+ channel antagonists. Pre-treatment of Guinea-pig and rat tissues with crude extract caused a rightward shift in carbachol- induced contractions, while in rabbit and rat tissues, crude extract shifted isoprenaline curves.	106
Linum usitatissimum	Alcoholic extracts of whole *Linum usitatissimum* (0.1, 0.2, 0.4 and 0.8 ml)	Guinea-pig ileum	The alcoholic extracts produced spasmogenic effect on the isolated ileum	107
	Flaxseed extract	Mice *in vivo* and isolated rabbit jejunum preparations	Flaxseed extract reduced the diarrheal score in mice, by 39%, 63.90% and 68.34% at the respective doses of 100, 300 and 500mg/kg. Intestinal secretions were reduced by 24.12%, 28.09% and 38.80%, and intestinal motility was reduced by 31.66%, 46.98% and 56.20% at	108

			respective doses of 100, 300 and 500mg/kg. Flaxseed extract produced a dose-dependent inhibition of both spontaneous and high K^+ (80mM)-induced contractions, and shifted the concentration-response curves of Ca^{++} to the right with suppression of the maximum response.	
Lythrum salicaria	The effects of hexane, chloroform, ethyl acetate, and 50% ethanol in water extracts of *Lythrum salicaria*	Isolated guinea pig ileum	The hexane, chloroform, ethyl acetate and 50% ethanol in water extracts (10 µl/5 ml organ bath) produced contractile effects. The largest contractions were elicited by the 50% ethanol in water extract.	109
	The n-hexane, chloroform, ethyl acetate and 50% ethanol in water extracts of the air-dried flowering parts of *Lythrum salicaria*	Guinea- pig ileum	The results showed that *Lythrum salicaria* extracts possessed moderate muscarinic receptor agonistic effect in Guinea pig ileum. The most prominent response was triggered by the 50% ethanol in water extract in a concentration-dependent manner. Atropine, indomethacin and PPADS plus suramin significantly reduced the contractile response caused by this extract.	110
Mangifera indica	Methanolic extract of the fruit seeds	Rabbitjejeinum and rat fundus strip	The extract showed a potent relaxnat activity on isolated rabbit jejunum that was refractory to the adrenergic blockers propranolol and tolazoline. Prior adminstration of the extract, physiologically blocked the stimulant effect of histamine on rat fundus strip.	111-112
Marrubium vulgare	Hydroalcoholic extract of the roots and aerial parts	Several smooth muscle preparations	The extract possessed a significant antispasmodic activity, it inhibited the action of acetylcholine, bradykinin, prostaglandin E2, histamine and oxytocin, with putative selectivity for cholinergic contractions	113-114
Matricaria chamomilla	Crude aqueous-methanolic extract	Isolated rabbit jejunum	The extract caused dose-dependent (0.3-3 mg/ml) relaxation of spontaneous and low K^+ (25 mM)- induced contractions of the isolated rabbit jejunum, while it exhibited weak inhibitory effect on high K^+ (80mM). The inhibitory effect of the extract on low K^+- induced contractions was partially inhibited in the presence of glibenclamide, while completely blocked by 4-aminopyridine.	115
Melissa officinalis	The leaves oil	Ileal smooth muscle	possessed relaxant effects on the guinea pig ileal smooth muscle	116
	The essential oils and citral	Rat ileum response	Inhibited the rat ileum response to KCl, ACh and 5-HT in a concentration dependent manner.	117
	Hydroethanolic leaf extract	Different segments of the gastrointestinal tract of mice	The extract possessed site- and dose-dependent effects on the contractile activity of the gastrointestinal tract, the motility response being impacted in the jejunum and ileum but not in the antrum and colon	118

Mentha longifolia	Crude extract	Isolated rabbit jejunum preparations	The crude extract caused inhibition of spontaneous and high K^+ induced contractions, with EC50 values of 1.80 (1.34–2.24) and 0.60 mg/ml (0.37–0.85), respectively. The results suggested spasmolytic activity, mediated through calcium channel blockade which further confirmed that the extract caused a rightward shift in the Ca++ concentration- response curves, similar to verapamil.	119
	Leaf hydroalcoholic extract	Rats ileal preparation	The results showed that KCl-, carbachol and BaCl2- induced ileal contractions were inhibited ($P<0.001$) by cumulative concentrations of the extract with the same potency. The extract (0.25-1 mg/ml) inhibited ($P<0.01$) ileal contractions induced by CaCl2 (0.45-2.7 mM) in a concentration- related manner. The antispasmodic effect of the extract was not affected by propranolol, N omega-nitro-L-arginine methyl ester and naloxone.	. 120
Mirabilis jalapa	The extract of the flowers (1-1000 mug/ml)	Gut smooth muscle	The extract exhibited an inhibitory effect (IC50 18±0.7 micorg/ml) on gut smooth muscle contractility.	121
Morus nigra	Phenolic compounds	isolated rat ileum	Phenolic compounds (kuwanon U, moracin O and albanol B) showed strong antispasmodic effects on isolated rat ileum	122
	Crude extract	Rabbit jejunum, guinea-pig ileum	The extract and its chloroform fraction inhibited carbachol- induced contractions of rabbit jejunum more potently than high K+ (80 mm). In Guinea-pig ileum, the extract and its aqueous and ethyl acetate fractions, exhibited atropine-sensitive gut stimulant activity	123
Myrtus communis	Crude methanol extract	Isolated rabbit jejunum	The crude methanol extract caused complete relaxation of spontaneous and K^+(80 mM)-induced contractions in isolated rabbit jejunum. It caused right ward parallel shift of calcium concentration response curves.	124
Nerium oleander	Crude extract	Guinea pig ileum	The extract potentiated both spontaneous and electrically evoked contractions of guinea pig ileum, this effect was not antagonized by the adrenergic blocker (tolazoline).	125-126
Nigella sativa	Aqueous extract of the seed	Guinea pig ileum	The extract exerted mild to moderate dose dependent relaxant effects of the ileum, and its spasmolytic activity was mediated through calcium antagonist effect.	127
	Volatile oil and ethanol extract	Rabbit jejunum	Inhibited spontaneous movements of rabbit jejunum. The calcium channel blockade was suggested as spasmolytic mechanism.	128

Table 3 Medicinal plant affected vascular smooth muscle contractility

Medicinal plant	Extract or compounds	Model	Action	Ref
Allium sativum	Raw garlic, several extracts and polysulfides	Experimental and clinical studies	Garlic-derived polysulfides stimulate the production of the vascular transmitter and enhance the regulation of endothelial nitric oxide (NO), which induce smooth muscle cell relaxation, vaso-dilation, and BP reduction. Garlic induced significant reduction in systolic and diastolic blood pressure due to a direct relaxant effect on smooth muscles.	129-136
Ammi visnaga	Visnadine	Rat aortic ring and portal vein segment	It was selectively inhibited the contractile response in the rat isolated aortic ring and portal vein segment. It caused nonspecific inhibition of vascular smooth muscle.	137-139
	Visnadine	In isolated guinea-pig hearts	Visnadin, 60.0 μg/ml or 120.0 μg/ml, increased coronary blood flow in isolated guinea-pig hearts by 46% and 57% respectively	140
	Khellin, visnagin or crude mixture of the *Ammi visnaga*	Clinical	Khellin, visnagin or crude mixture of the *Ammi visnaga* active principles have a direct muscle relaxant. Oral preparation is used to dilate the coronary arteries efficiently in angina pectoris	141
Arundo donax	Alkaloid gramine extracted from the plant	In dogs	It possessed vasopressor activity, raising the blood pressure in dogs after small doses and causing a fall in larger doses.	61, 142
	A defatted ethanolic extract of the rhizomes	Rats	It produced hypotensive effect	60-61
Capparis spinosa	Aqueous extract	Aortic rings of rats	Adding of *Capparis spinosa* aqueous extract (CSAE)during the plateau phase of contraction, induced by noradrenaline and KCl, produced a rapid relaxation. Incubation of aortic ring with CSAE during 30 min shifted the noradrenaline induced dose response curve ($p<0.001$), the maximum response ($p<0.001$) was attenuated which indicating that antagonistic effect of the α1-adrenoreceptors was non-competitive.	143-144
	Aqueous extract of different parts (roots, leaves, stems, flowers, fruits and kernels)	Thoracic aorta rings and windpipe of rat	Addition of extracts during the stage of contraction led by the phenylephrin for the thoracic arteries showed a light vasodilatation. Incubation (30 min) with extracts showed a significant vasodilator effect for fruits and kernels, and vasoconstrictor effect for leaves.	145
Cassia occidentalis	Aqueous extract of the leaf	Rat aortic rings	The extract inhibited contraction elicited by noradrenaline (NA) and potassium chloride (KCI). It also relaxed aortic rings pre-contracted with 10^{-7} M NA and 50m M KCI. The relaxation did not require the presence of an intact vascular endothelium and was not affected by indomethacin and methylene blue.	146
Cichorium intybus	A diester composed of	Rat aorta strips	This compound did not affect contraction induced by a high concentration of potassium (60 mM K^+),	147-148

	(S,S)-tartaric acid and caffeic acid isolated from the plant		while it inhibited NE-induced vaso-contraction in the presence of nicardipine. The inhibition of vaso-contraction is due to a decrease in calcium influx from the extracellular space, which enhanced by NE.	
Cistanche tubulosa	Echinacoside , a phenylethanoid glycoside isolated from *Cistanche tubulosa*	Rat thoracic aortic rings	Echinacoside mediates the endothelium-dependent vasodilator action in rat thoracic aortic rings through nitric oxide (NO)-cGMP pathway.	149
	Methanolic extract from the dried stems	Rat aortic strips	It showed inhibitory effect on contractions induced by noradrenaline in isolated rat aortic strips. Kankanoside F, kankanose, echinacoside, acteoside, and cistanoside F, which isolated from the extract were responsible for thevasorelaxant activity.	150-151
Citrus aurantifolia	Aqueous extract	*In vivo*, rabbits and in vitro rat aortic strips	The extract possessed anti-hypertensive activity by cardio-depression and vaso-relaxation. It evoked vaso-relaxant effects which totally abolished by removal of the endothelium layer or by a pre-treatment with L-NAME	152-153
Convolvulus arvensis	Ethanolic and aqueous extracts	Rabbit aortic rings	It appeared that calcium-dependent K channels (BKCa) has a partial role in the relaxing effect of the ethanolic extract, but not aqueous extract. However, with the using of high K^+ Krebs, both extracts exhibited relaxant effect due to reducing the entry of calcium ions from outside. The adrenergic receptor α1 has a role but with different magnitude between the extracts, with high degree for aqueous extract, that reduced the maximum response (E_{max}) of aortic rings to phenylephrine, and this was similar to the effect of α1-blocker (prazosin).	154-156
Cordia myxa	Fruit mucilage at different stages of maturity	*In vivo*, rabbit	It caused hypotensive effect and respiratory stimulant effect. The hypotensive effect was due to activation of parasympathetic ganglia and dilatation of peripheral blood vessels, whereas the respiratory stimulant effect was due to activation of chemoreceptors in the aortic arch and carotid body.	157
Equisetum arvense	Dicaffeoyl -meso-tartaric acid from *Equisetum arvense*	Rataorta strips	It showed slow relaxation activity against norepinephrine (NE)-induced contraction of rat aorta with/without endothelium. This compound did not affect contraction induced by a high concentration of potassium (60 mM K^+), while it inhibited NE-induced vaso-contraction in the presence of nicardipine.	158-159
Hibiscus sabdariffa	Extract of dried and powdered calyces	Rat thoracic aorta	The crude extract induced mainly endothelium-dependent relaxant effects via NOS activation	160
Leontice leontopetalum	Low conc. of petaline chloride, a quaternary alkaloid from	Isolated aorta	Caused relaxation of the epinephrine-contracted aorta. Larger concentrations (up to 3 mg/ml) caused nonsustained large contractions of the	161

	Leontice leontopetalum		aorta. The contractile effects were not inhibited by atropine	
	Oblongine chloride (3 x 105-10-3 M), a quaternary alkaloid from *Leontice leontopetalum*	Guinea -pig isolated main pulmonary artery rings	Caused concentration-dependent relaxation of epinephrine-pre-contracted guinea-pig isolated main pulmonary artery rings. The effect was not affected by propranolol or by indomethacin but was significantly attenuated by pre-treatment with 3 x 10-5 M ATP and potentiated by pretreatment with quinacrine(10-5 M).	162
Marrubium vulgare	The crude extracts of the aerial parts	Rat aorta	The extract strongly inhibited the *in vitro* KCl-induced contraction of rat aorta. Furanic labdane diterpenes, marrubenol and marrubiin were the most active compounds.	163
	Crude extract	Rat aorta	The extract inhibited the contractile responses of rat aorta to noradrenaline and to KCl (100 mM). Inhibition was greater in aorta from spontaneously hypertensive rats compared to normotensive rats and was not affected by the NO synthase inhibitor.	164
	Marrubenol (a diterpenoid extracted from *Marrubium vulgare*)	rat aorta	Marrubenol inhibited the contraction of rat aorta evoked by 100 mM KCl (IC50: 11.8±0.3 microM, maximum relaxation: 93±0.6%) than of the contraction evoked by noradrenaline (maximum relaxation: 30±1.5%) in rat aorta. It also simultaneously inhibited the Ca^{2+} signal and the contraction evoked by 100 mM KCl, and decreased the quenching rate of fura-2 fluorescence by Mn^{2+}.	165
Melilotus officinalis	Crude extract	Rabbit , *in vivo*	The extract caused hypotensive and vaso-dilating actions due to the vascular smooth muscle relaxation in rabbits.	166-167
Melissa officinalis	Aqueous extract	Isolated rat aortic rings precontracted with phenylephrine	The extract and rosmarinic acid isolated from the extract possessed vasorelaxant effect, entirely dependent on the presence of endothelium and was abolished by pretreatment with L-NAME, while pretreatment with indomethacin and glibenclamide reduced the relaxation to a minor extent	168
Mentha longifolia	Crude extract and fractions	Rat and rabbit aortic rings	In rat aortic rings, the crude extract and aqueous fraction-induced endothelium-dependent atropine-sensitive vasodilator effect. In rabbit aortic rings, crude extract relaxed phenylephrine (1 μM) and high K+ (80 mM) pre-treated ring. Chloroform fraction was more potent against high K+, similar to verapamil and caused a rightward shift in the Ca++ concentration response curves. Aqueous fraction partially relaxed high K+ pretreated ring.	169
Morus alba	Leaves extract	Isolated rat thoracic rings	The extract possessed dual vasoactive effects, and the relaxation was greater than the contraction. The relaxation was mediated by inhibition of voltage- and receptor-dependent Ca2+ channels in vascular smooth muscle cells, while the contraction occurred via activation of ryanodine receptors in the sarcoplasmic reticulum.	170

Myrtus communis	Crude methanol extract	Isolated rabbit aorta preparations	The crude methanol extract caused relaxation of phenylephrine (1 μM)- and K^+(80 mM)-induced contractions in isolated rabbit aorta preparations, similar to verapamil.	171
Nigella sativa	Aqueous seed extract	Rat aortic ring	Incubation with the aqueous seed extract during 30 min caused a right shift of the contraction response curve of aortic ring to norepinephrine with a reduction of the maximal contraction response ($P<0.01$). Endothelium destruction significantly reduced the vaso-relaxant effect of the extract at a dose of 30 mg/ml ($P<0.01$).	172
Olea europaea	Oliv e oil	Rat aortic ring preparation	The maximum contraction of aortic ring preparations in response to phenylephrine (10-6 m) was significantly decreased in hypertensive rats fed with olive oil. The relaxant responses to acetylcholine (10^{-5}m) were significantly enhanced in the rings from hypertensive rats treated with olive oil. Olive oil attenuated the dose-response curves induced by phenylephrine (10^{-8}-10^{-5} m) from hypertensive rats, accompanied with a slower contraction.	173
Orchis mascula	Crude extract	Isolated rabbit aorta	The crude extract caused concentration-dependent relaxation of both phenylephrine and high K^+ (80mM)- induced contractions and caused a rightward shift of the calcium concentration–response curves similar to the effect of verapamil.	174-175

Table 4 Medicinal plant affected uterine smooth muscle contractility

Medicinal plant	**Extract or compounds**	**Model**	**Action**	**Ref**
Arundo donax	A defatted ethanolic extract of the rhizomes	Rats	It produced hypotensive and antispasmodic effects against histamine, serotonine and acetylecholine induced spasms. Bufotenidine showed three main pharmacological actions, anti-acetylecholine effect, histamine release and uterine stimulant effects.	61, 142
	Bufotenidine	Rats	Bufotenidine showed three main pharmacological actions, anti-acetylecholine effect, histamine release and uterine stimulant effects.	61-142
Capsella bursa-pastoris	A purified substance from an alcohol extract	Rat uterus	It exerted contractile activity on the rat uterus which was similar to that of oxytocin. The effective substance had some characteristics of a polypeptide.	176
	Aqueous extract	Isolated rabbit and guinea pig uterine horn	Water extracts (infusions) from a group of medicinal plants including *Capsella bursa-pastoris* enhanced the uterine tonus in isolated rabbit and guinea pig uterine horn.	177
	Tea infusion	Clinical	The plant was used in the treatment of menorrhagia and metrorrhagia, which seem to be mediated through an increased contraction of smooth muscles and uteromimitic effect. As a tea-like infusion, the	178

			recommended dose is 2 g to 4 g in 150 ml of water after boiling for 15 minutes.	
Daturametel	Leaf and root extracts	Rat uterus and rectum smooth muscles	The leaf extract and scopolamine showed antispasmodic effects, while root extract and acetylcholine caused contraction of the isolated rat uterus and rectum whole muscle. The results indicated that the plant contained antispasmodic and spasmogenic constituents.	179-180
Daucus carota	Anitrogen containing tertiary base isolated from the seeds	Ileum, uterus, blood vessels and trachea of different species of animals	The tertiary base possessed papaverine like nonspecific smooth muscle relaxant and spasmolytic activity, but its activity was found to be about one-tenth of that of papaverine.	181-182
Erodium cicutarium	Several organic extracts	Rat uterus	All extracts had a spasmogenic action on isolated uterus preparation of the rat. The methanol extract produced regular monophasic contractions of the quiescent uterus, which ceased immediately when the tissue was washed.	83-86
Hibiscus sabdariffa	Aqueous extract	Rat bladder and uterus	extracts induced rat bladder and uterine contractility in a dose-dependent manner via a mechanism unrelated to local or remote autonomic receptors or calcium channels	41
	Aqueous extract	Rat uterus	inhibited the tone rhythmically contracting rat uterus	41
Luffa cylindrical	Aqueous extracts of *Luffa cylindrica* leaves	Isolated rat uterus	the extract increased rat uterine motility.	183
Mangifera indica	Methanolic extract of *Mangifera indica* fruit seeds	Isolated uterus	It inhibited the spontaneaous activity of the uterine muscle and effectively antagonised the stimulant activity of acetylcholine on the muscle.	184
	Aqueous extract of Mango kernel	Virgin rat Uterine smooth muscle	The extract significantly decreased the strength, frequency and contractile activity of uterine smooth muscle, but the contractile activity was returned to the basal level at the concentrations of 200 and 2000 µg/ml. The effects might not be through cholinergic muscarinic receptors and atropine could enhance the effects of the extract on frequency through other receptors	185
Capsella bursa-pastoris	Extract of dried or green plant	Guinea - pig uterus	The extract of dried or green plant causes strong contraction of uterus of guinea pig. A quarternary ammonium salt has been isolated from the herb which is reported to be responsible for this activity.	70
Momordica charantia	The seeds of the plant	*In vivo*, mice and rats	The seeds induced abortions in rats and mice, and the root possessed uterine stimulatory effects.	186-189

2. Conclusion

The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine for some aspect of primary health care. We still need herbal medicines to relax the uterine muscles in cases of abortion, or to increase uterine contractions to enhance delivery. Spasmolytic drugs are required to relieve gastrointestinal colic, while drugs which relax bronchial smooth muscles are needed in asthmatic attacks. This review was designed to discuss the plants which possessed biological activity on smooth muscles to encourage the research in this direction to introduce new drugs characterized by therapeutic efficacy and safety.

Compliance with ethical standards

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Disclosure of conflict of interest

The author confirms that there is no conflict of interest.

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