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Chemical Constituents and Pharmacological Effects of *Lathyrus sativus* – A Review

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Abstract: *Lathyrus sativus* contained starch, cane sugar, leguminvicilin, legumelin, fixed oil, gum resin, oleo-resin, alkaloids, carbohydrates, flavonoids, terpenes, phenols, tannins, vitamin C, riboflavin, carotenoids, beta-carotene, proteins and amino acids. It possessed many pharmacological effects included antioxidant, nervous, antidiabetic, analgesic, antipyretic and cardioprotective effects. The current review discussed the chemical constituents and pharmacological effects of *Lathyrus sativus*.

Keywords: constituents, pharmacology, *Lathyrus sativus*, toxicity

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I. INTRODUCTION

Abstract:
In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. The pharmacological studies showed that medicinal plants possessed wide range of pharmacological effects. Medicinal plants extracts were an important source of chemicals which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives(1-35). *Lathyrus sativus* contained starch, cane sugar, leguminvicilin, legumelin, fixed oil, gum resin, oleo-resin, alkaloids, carbohydrates, flavonoids, terpenes, phenols, tannins, vitamin C, riboflavin, carotenoids, beta-carotene, proteins and amino acids. It possessed many pharmacological effects included antioxidant, nervous, antidiabetic, analgesic, antipyretic and cardioprotective effects. The current review will highlight the chemical constituents and pharmacological effects of *Lathyrus sativus*.

Plant profile:
Synonyms: *Lathyrus asiaticus*, *Lathyrus sativus* subsp. Asiaticus(36).
Taxonomic classification:
Kingdom: Plantae, **Subkingdom**: Viridiplantae,**Infrakingdom**: Streptophyta, **Superdivision**: Embryophyta, **Division**: Tracheophyta, **Subdivision**: Spermatophytina, **Class**: Magnoliopsida, **Superorder**: Rosanae, **Order**: Fabales, **Family**: Fabaceae, **Genus**:*Lathyrus*and **Species**: *Lathyrus sativus*(37).

Common names:
Arabi: Hortuman, Gelban**; Bangladesh**: Khesari; **Burma**: Pé-kyin-baung, pé-sa-li, mutter pea; **China**: San lee dow; **English**: Grass pea, chickling pea, Chickling vetch, Dogtooth pea, grass peavine, Indian pea, Riga pea, Wedge peavine; **French**: Gesse, gesse blanche, gesse commune, poiscarré, lentilled'Espagne; **German**: Saat-Platterbse, weisse Kicher, Kicherling; **India:** Kesare, khesari, karas, karil, kasar, khesari dhal, khesra, lang, chural, latri, lakhori, Lakhodi, chattramatur, santal, teora, tiuri, batura, chickling vetch, chickling pea; **Italy**: Cicerchiacoltivata, pisellobretonne, pisellocicerchia; **Nepal**: Kheshari; **Norwegian**: erteknapp; **Pakistan**: Matri, mattra; **Portuguese**: chícharo, sincho; **Spanish**: almorta, guija, muela, tito, chícharo; **Swedish**: åkervial; **Turkish**: akburçak, mürdemek, mürdümük(38-39).

Distribution:
Some of the earliest archaeological evidence showed that the plan was domesticated in (Jarmo, Kurdistan, dated at 8000 BC**)** in Iraqi and in (Ali Kosh, dated at 9500-7600 BC) and (TepeSadz dated at 7500-5700 BC) in Iran. However, the plant was domesticated in the Balkan region in the early Neolithic age. It domesticated in Europe around 6000 BC and have been found in India dating to 2000-1500 BC. Today, grass pea is widely cultivated in Asia, (especially in China, Bangladesh, India, Nepal, Pakistan, Kazakhstan,

Uzbekistan and the Middle East), southern Europe and North Africa and to a lesser degree America, Australia and South Africa[39-41].

Description:

Grass pea is a much branch sub-erect, straggling or climbing herbaceous winter annual; stems are 0.6-9.0m tall and the leaves are pinnately compound with usually two leaflets (linear-lanceolate 25–150 mm long, 3-9 mm broad). The upper leaflets have modified tendrils. Flowers are solitary, axillary and are borne on peduncles 30-60 mm long; corolla 12-24 mm long, and are reddish purple, pink, blue or white. Pods are oblong, 2.5-4.00 cm long, flat and slightly curved and each pod has 3-5 seeds that are white, grayish-brown or yellowish and usually spotted or mottled[39, 42].

II. TRADITIONAL USES

The seeds oil was used medicinally as a powerful cathartic. It was also used in Bangladesh to cure scabies, eczema and allergy. Immature pods were cooked and eaten as a vegetable, or boiled, salted and consumed as a snack. Young vegetative parts were cooked as a green vegetable; they were also dried for off-season use as a vegetable in Asia. In India, the whole seeds were sometimes boiled, but were most often processed into dhal. The flour, made by grinding either the whole or split seeds, was sold as (besan). Grass pea was sometimes used to adulterate more expensive pulses, such as chickpea or pigeon pea. In Bangladesh (roti) made out of grass pea flour was a staple for landless labourers. In Ethiopia and Eritrea grass pea seeds were mainly consumed in the form of sauces (wot), shirowot (sauce made of flour) and kikwot (sauce made of hulled split seeds) and were eaten together with injera (a pancake-like unleavened bread). Boiled grass pea seeds (nifro) were also consumed in most areas, whereas kitta (an unleavened bread) made from grass pea seeds was consumed mainly during times of acute food shortage. Young grass pea plants were used as fodder for cattle or for grazing in many countries. As fodder, the plants can be eaten green or as hay[39, 42-46].

III. PARTS USED:

Immature pods, young vegetative parts flour, seeds and seed oil[42-46].

Chemical constituents:

Lathyrus sativus seeds contained starch, cane sugar, leguminvicilin, legumelin, fixed oil, gum resin, oleo-resin, alkaloids, carbohydrates, flavonoids, terpenes, phenols, tannins, vitamin C, riboflavin, carotenoids, beta-carotene, proteins and amino acids [47-49].

The analysis of composition of four samples of grass pea seeds showed that the plant seeds contained water 7.5-8.2%, starch 48.0-52.3%, protein 25.6-28.4%, acid detergent fiber 4.3-7.3%, ash 2.9-4.6%, fat 0.58-0.8%, calcium 0.07-0.12 mg/kg, phosphorus 0.37-0.49 mg/kg, lysine 18.4-20.4 mg/kg, threonine 10.2-11.5 mg/kg, methionine 2.5-2.8 mg/kg and cysteine 3.8-4.3 mg/kg[39, 50].

However, analysis of *Lathyrus sativus* seed samples from states of Bihar, Chattisgarh, West Bengal, Orissa and Andhra Pradesh in India, showed that the seeds contained: moisture 8.38 - 10.45%, crude protein 22.79- 28.26%, crude fiber 4.95- 15.22%, total ash 2.29-3.31%, nitrogen free extract 56.27-70.91%, ether extract 0.68- 1.50% and energy 330-403 (Kcal)[51-52]. While, analysis of *Lathyrus sativus* seed samples from Ethiopia, showed that the seeds contained 27.29±0.13 to 31.98±1.25 % protein, 1.17±0.02 to 3.63±0.9 5% ash, 0.92±0.01 to 1.47±0.07% fat, 3.56± 0.54 to 8.62 ±0.93% crude fiber, 55.05±2.57 to 65.17±0.72% carbohydrates, 347.47±13.8 6 to 384.93±3.56 Kcal/100g energy, 82.01±11.79 to118.97±23.48 mg/100 g calcium, 98±17 to 178 ±89 mg/100g magnesium, 242±27 to 432±93 mg/100g phosphorus, 2.74±0.5 to 4.52 mg/100g zinc, 4.64±0.4 to 8.74±2.56 mg/100 g iron, 1.16±0.14 to 1.78±0.27 mg/100g manganese and 0.85±0.10 to 1.23±0.30 mg/100 g copper[53].

Leaf contained moisture 84.2%, crude protein 6.1%, fat (ether extraction) 1.0%, carbohydrates 7.6%, ash 1.1%, calcium 0.16%, phosphorus 0.1%, iron 7.3 mg/100g, and carotene (as vitamin A), 6,000 IU/100g. Analysis of green grass pea at the flowering stage on a dry weight basis revealed: protein: 17.3%, fiber: 36.6%, fat: 4.47%, ash: 6.0%, P_2O_5: 0.51% and CaO: 1.08%[42].

Comparison of common amino acid (g/16g) of *Lathyrus sativus* protein were: alanine 3.19- 9.82, arginine 3.29- 21.4, aspartic acid 8.53- 27.6, cystine 0- 4.50, glutamic acid 13.40- 39.5, glycine 3.45- 9.70, histidine 2.22- 6.61, isoleucine 3.41- 9.77, leucine 5.69- 15.9, lysine 4.08- 16.7, methionine 0.24- 0.82, phenylalanine 2.95-10.6, proline3.07-9.50, serine 0-10.9, threonine 2.59- 8.43, tyrosine 1.44- 6.07, and Valine3.91- 12.2[54].

protein content was 27.0 ± 2.39, 27.0 ± 1.99 and 26.7 ± 1.90 gm/100 gm in samples collected from Bilaspur, Durg and Raipur districts of Chhattisgarh State, India, respectively. Arginine content was high in split grass pea (SGP) and sulphur containing amino acids (cysteine and methionine) were less than other amino acids. However, amino acid composition in samples collected from three districts were: essential [threonine 3.40 ± 0.10, valine 5.00 ± 0.03, methionine 0.76 ± 0.07, isoleucine 4.25 ± 0.02, leucine 7.06 ± 0.02, phenylalanine 4.50

± 0.11, histidine 2.41 ± 0.06, lysine 6.40 ± 0.17 and tryptophan not reported; non essential [aspartic acid 10.51 ± 0.09, serine 5.14 ± 0.08, glutamic acid 17.83 ± 0.14, proline 8.71 ± 0.09, glycine 3.95 ± 0.07, alanine 4.30 ± 0.08, cystine 0.91 ± 0.01, tyrosine 3.22 ± 0.03 and arginine 8.92 ± 0.19][(55)].

Condensed tannin levels in *Lathyrus sativus* ranged from 0 to 4.38 g/kg. The total phenolics ranged from 39 to 999 mg/kg. Both condensed tannins and total phenolics were highly correlated with the seed coat pigmentation. Coloured genotypes containing greater levels of tannin. High levels of trypsin inhibitor was also recorded in grass pea. Trypsin inhibitor activity (TIA) values varied from 15.53 to 18.99 TIU/ mg[(56)].

Fatty acid compositions of 173 different grass pea accessions have been studied. The results indicated that total saturated fatty acids, total monounsaturated fatty acids, total polyunsaturated fatty acids, and total fatty acids ranged from 295.72 to 436.94, 113.19 to 170.78, 127.39 to 179.39 and 538.04 to 778.98 mg/100g, respectively. The unsaturated fatty acids, oleic acid, linoleic acid, γ-linolenic acid, and α-linolenic acid were the main components of fatty acids, ranged from 109.22 to 163.95, 59.57 to 82.98, 16.18 to 30.38, and 45.56 to 71.59 mg/100g, respectively[(57)].

A neurotoxin, ß-N-oxalyl-L-a, ß-diaminopropionoc acid (ODAP also known as BOAA) has been identified as the causative principle for lathyrism. ODAP was found in all tissues of *Lathyrus sativus* plants, irrespective of age or variety[(39)]. Its concentrations vary widely (from 0.2 to greater than 1.01 mg/g of seed) among a total of 1262 accessions collected from India and Ethiopia, the ODAP distribution in embryo was the greatest (400mg/g) followed by cotyledon (126 mg /g), seed coat (81 mg /g), stem (64 mg /g), leaf (60 mg /g), pod (24 mg /g) and root (14 mg /g)[(55. 58)].

The phenolic compounds were extracted from 30 varieties of grass pea (*Lathyrus sativus*) into 80% (v/v) methanol. Total phenolic contents ranged from 1.88 to 7.12 mg/g extract and 20.3 to 70.3 mg/100 g seeds. Two derivatives of p-coumaric acid were the dominant phenolic compounds[(59)]

Common anti-nutritional factors: protease inhibitors (trypsin inhibitor), amylase inhibitors, lectins, saponins, phytic acid, and the oligosaccharides of raffinose family, were recorded in *Lathyrus sativus*. They vary greatly from variety to variety and they influenced by season, processing method and storage[(56, 60)].

IV. PHARMACOLOGICAL EFFECTS

Antioxidant effects:

The antioxidant activity of *Lathyrus sativus* was determined using DPPH scavenging activity, reducing power, β-carotene bleaching inhibition and TBARS formation inhibition. *Lathyrus sativus* showed high concentration of flavonoids and antioxidant activity [DPPH scavenging activity : 18.95 ±0.64 soaked and 15.23 ± 0.48 mg/ml cooked; Reducing power: 3.94 ± 0.06 soaked and 3.26 ± 0.11 mg/ml cooked; β-carotene bleaching inhibition: 0.92 ±0.16 soaked and 0.82 ± 0.08 mg/ml cooked, and TBARS inhibition: 3.47 ± 0.25 soaked and 1.62 ± 0.09 mg/ml cooked][(61)].

The antioxidant activity of *Lathyrus sativus* extracts were determined using Folin-Ciocalteu's phenol reagent, 2,20-azinobis-(3-ethylbenzothi azoline-6-sulfonic acid (ABTS) and ferric-reducing antioxidant power (FRAP) methods. The extracts and seeds were characterized using Trolox equivalent antioxidant capacity values of 0.015–0.037 mmol Trolox/g extract and 0.158–0.372 mmol Trolox/100 g seeds, and FRAP values of 0.045–0.120 mmol Fe^{2+}/g extract and 0.487–1.189 Fe^{2+}/100 g seeds. The results of the ABTS (r = 0.881) and FRAP (r = 0.781) assays were correlated with the total phenolics content[(59)].

Antiradical and total antioxidant activities of extracts from raw, prepared for inoculation, fermented (tempeh) and cooked seeds of grass pea (*Lathyrus sativus*) were measured. Tempeh fermentation with *Rhizopus oligosporus* resulted in higher scavenging activity towards DPPH and ABTS+ radicals which correlated well with the content of total phenols. In Derek cultivar, fermentation caused a significant inhibition of linoleic acid oxidation by methanol extracts. In buffer extracts the highest TAA values were observed in raw seeds. Cooking of seeds lowered RSA values as compared to fermentation, especially for the DPPH assay[(62)].

Extracts of grass pea flour were investigated for the radical scavenging capacity using ABTS and DPPH assays. Extracts of grass pea flour possessed a weak conversion of the DPPH radical, estimable in a reduction of 36.3% at the highest tested dose. The flour extracts showed a moderate reducing capability of ABTS radical cation. The activity became remarkable at 250 µg/ml as the ABTS radical cation reduction was 47.1%[(52)].

Nervous effect:

The CNS depressant activity of the methanolic extract of *Lathyrus sativus* seeds (200 and 300 mg/kg bw) was evaluated in mice using open field and hole-cross method. The methanolic extract significantly ($p < 0.001$) decreased the locomotor activity of mice in open field and hole-cross method at both the tested doses (200 and 300 mg/kg) which were comparable to the standard drug, diazepam (1 mg/kg)[(47)].

The effect of *Lathyrus sativus* collected from Andhra Pradesh, Odisha, Kerala, West Bengal, Chhattisgarh and Bihar (raw, wet roasted, boiled and soaked + boiled) and diazepam (2 mg/kg, ip) on the coordinated motor movement was assessed using Rota-rod test in rats. The soaked + boiled processed seeds showed a better muscle co-ordination activity compared to the other processed *Lathyrus sativus* seeds. The improved muscle coordination activity with processed seeds of soaked + boiled might be due to their decreased ODAP and tannin levels. The better agroclimatic conditions might be responsible for good muscle coordination activity showed by the samples collected from Andhra Pradesh[(63)].

The action potential in amphibian sciatic nerve *in vitro* was abolished by the topical application of *Lathyrus sativus* seed extract. It probably caused by the high K^+ content of the seed extracts[(64)].

Analgesic and antipyretic effects:

The analgesic activity was studied using acetic acid induced writhing and formalin induced paw licking methods in mice, while 2,4-dinitrophenol (DNP) induced pyrexia model was used to investigate the antipyretic activity in mice. The plant extracts significantly ($p < 0.001$) inhibited the writhing induced by acetic acid in mice to 87.09% and 80.65% (at 200 and 300 mg/kg respectively) compared to the standard indomethacin (70.97%). The extracts (200 and 300 mg/kg respectively) also significantly ($p<0.001$) reduced the writhing to 43.39%, 64.15% in early and 46.15%, 97.44% in late phase of formalin-induced licking and biting. In 2,4-DNP induced pyrexia the extracts exhibited protection at 200 and 400 mg/kg, similar to standard drug aspirin at 150 mg/kg[(47)].

Antidiabetic effect:

Lathyrus sativus showed antihyperglycemic, the methanolic extract of non-boiled and boiled *Lathyrus sativus* seeds extract, significantly and dose-dependently reduced blood glucose concentrations in glucose-loaded mice. The reductions in blood glucose levels at extract doses of 100, 200 and 400 mg/kg of non-boiled seeds were 37.7, 44.8, and 48.8% respectively. The percent reductions in blood glucose levels with methanolic extract of boiled seeds were 31.0, 45.6, and 47.3% at the same doses respectively[(65)].

Cardioprotective effect:

The cardioprotectie effects of *Lathyrus sativus* seed flour was studied in myocardial infarction induced by isoproterenol (ISP) in rats. *Lathyrus sativus* seed flour was incorporated in the rats diet (30, 50 and 75%). The results showed that *Lathyrus* countered the adverse effects of ISP induced myocardial infarction to major extent suggesting its vasodilatation and inhibition of platelet aggregation and antioxidant potential owing to replenishment of antioxidant defenses and decreasing the ischemic injury due to presence of phenols and homoarginine[(66)].

Toxicity:

Lathyrism caused by *Lathyrus sativus*:

Heavy prolonged consumption of grass pea caused a motor system disease (Lathyrism) which was known to ancient Hindus, Hippocrates and ancient Greece[(67-68)]. Lathyrism is a disease caused by excessive consumption of grass pea, *Lathyrus sativus* especially under conditions of severe drought. Grass pea contains 3-N-oxalyl-L-2, 3-diaminopropanoic acid (β-ODAP) a putative neurotoxin which acts through excitatory mechanism causing neurolathyrism, in human and animals. In human, individuals of both sexes and all age groups can be affected but the disease is most prominent among young male adults. The symptoms of the disease usually begin suddenly few weeks or months after consumption of seeds of *Lathyrus sativus*. There may be very frequent urination (30-40 times during the night), prodormal sensory symptoms of pain, prickling numbness and cramps, but commonly the victim suddenly feels weak and heavy in the legs and loins, with tremulous muscles when weight is put on them. There is dragging of the legs, increased reflexes and impaired ability to walk. In mild cases, only ankle and knee joint movements were restricted by muscle spasm, causing the victim to walk rigidly on the balls of his feet, tilting the pelvis. The severely affected individual complained abductor spasticity, walk with a characteristic scissoring gait, and require support. The most severely affected ones develop tonic paraplegia in flexion and were compelled to crawl or use a wheel chair. Post-mortem examination showed pronounced atrophy of the spinal cord. Histological examination revealed disappearance of cells in the affected portion of the nervous system and increase in neuroglia. The affected muscles are atrophied and show fatty degeneration[(69-71)].

Lathyrism also occurred in domestic animals when took *Lathyrus*as fodder. Lathyrism was reported in many species including the duck, goose, hen, peacock, pig, ox, sheep, elephant and horse. Horse was the most susceptible to *Lathyrus sativus* toxicity . Horse developed symptoms of the disease after around 10 days when fed exclusively with *Lathyrus sativus* and after 2-3 months while diet contains partially *Lathyrus sativus.* Symptoms of the disease include paralysis of the hind legs accompanied by dyspnea and roaring. The disease may be more serious than in man with involvement of long peripheral nerves as well as spinal cord and brainstem. Death usually followed after months of illness with symptoms of asphyxia[(72)].

Bovines exhibit symptoms similar to those in horses except roaring. They showed suspended rumination, constipation, paralysis of the limb, weak pulse and loss of sensibility in the skin. Sheep, pigs, dogs, ducks, geese, peacocks and pigeons all develop weakness and paralysis with accompanying symptoms. Postmortem examination showed atrophy of the larynx muscles and degenerative changes in the ganglion cells of the spinal cord and vagal and accessory nuclei of the medulla. Thickening of the walls of the arterioles and capillaries in the spinal cord and degeneration of the myocardium, congested patches in the stomach and intestines, hyperaemia of the lungs and catarrhal bronchitis[(71)].

Regarding the mode of toxicity, several *in vitro* cell culture studies have established that L-ODAP is a glutamate receptor agonist. The convulsant actions of BOAA were principally mediated directly through A2/A3 glutamate receptor systems present on selected neurons. Furthermore, the cerebellum administration of low concentrations of BOAA exert *in vivo* activation of glutamate receptors involved in the regulation of cGMP level. Some studies suggest a free radical oxygen species (ROS) generation as a mechanism of ODAP toxicity in rats following its focal hippocampal application. Also, *in vitro* studies with mouse brain slices treated with ODAP suggest an inhibition of mitochondrial complex I (NADH dehydrogenase). Inhibition of tyrosine amino transferase (TAT) by ODAP both *in vivo* and *in vitro* suggested an alternative interesting mechanism of neurotoxicity. TAT is the only enzyme identified so far that is substantially inhibited by L-ODAP. C57BL/6J black mice gave ODAP treatment showed a significant increase in brain DOPA and other catecholamines[(73-76)].

The disease is usually non-progressive but irreversible. Further consumption of these peas should not be allowed. Tolperisone, a centrally acting muscle relaxant has been shown to produce significant reduction in the spasticity of neurolathyrism patients. The hypertonicity can to a certain extent be controlled by baclofen[(77)].

V. CONCLUSION

Lathyrus sativus possessed many pharmacological effects included antioxidant, nervous, antidiabetic, analgesic, antipyretic and cardioprotective effects. However, lathyrism is a disease caused by excessive consumption of *Lathyrus sativus* especially under conditions of severe drought. It contained 3-N-oxalyl-L-2, 3-diaminopropanoic acid (β-ODAP) a putative neurotoxin exerted its toxicity through excitatory mechanism causing neurolathyrism, in human and animals. The current review discussed the chemical constituents and pharmacological and toxicological effects of *Lathyrus sativus*.

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