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Therapeutic Importance of Hyoscyamus Species -A Review

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Abstract *— Among the 84 genera and over 3000 species that make up the family Solanaceae, Hyoscyamus stands out as one of the most significant and biggest. Hyoscyamine and scopolamine, two of the several tropane alkaloids, may be found in abundance in all Hyoscyamus species. Alkaloids, flavonoids, tannins, terpenes, saponins, carbohydrates, cardiac glycosides, and anthraquinones were all found in the phytochemical investigation of Hyoscyamus species. They had many different pharmacological effects, such as anti-diabetic, antioxidant, anticancer, insecticidal, antiasthmatic, antiallergic, antidiarrheal, antisecretory, Ca2+ channel-blocking, hypotensive, cardioprotective, hepatoprotective, antihyperuricemic, anti-Parkinsonian, anticonvulsant, antidepressant, and antihyperuricemic. The chemical composition, pharmacological activities, and toxicological dangers of Hyoscyamus species growing in Iraq were reviewed in this paper.*

Keywords *— **Hyoscyamus albus, Hyoscyamus niger, Hyoscyamus reticulates, chemical constituents, pharmacology, toxicology***

INTRODUCTION

Herbal medicine has been used by humans for thousands of years. Every civilization ever has relied on herbs. According to the WHO, almost 80% of people throughout the globe are now making use of herbal medicine as a kind of basic health care. Nonetheless, humans still rely on plants for some of the most effective medications (1-30). Alkaloids, flavonoids, tannins, terpenes, saponins, carbohydrates, cardiac glycosides, and anthraquinones were all found in the phytochemical investigation of Hyoscyamus species. They exerted many pharmacological effects included anti-diabetic, antioxidant, anticancer, insecticidal, antiasthmatic, antiallergic, antidiarrhoeal, antisecretory, Ca2+ channel-blocking, hypotensive, cardioprotective, hepatoprotective, antihyperuricemic, Anti-Parkinsonian, anticonvulsant, antidepressant, in addition to anticholinergic effects of tropane alkaloids. The goal of this analysis was to provide insight on the chemical make-up, pharmacological actions, and toxicological dangers of Hyoscyamus species native to Iraq.

Plant profile:

Synonyms:

Species of the genus Hyoscyamus include the canariensis (Ker Gawl.), clusii (G. Don), luridus (Salisb.), major (Mill), minor (Mill), and varians (Hyoscyamus) species. Vis Plant genus: Hyoscarpus niger Dulac, The scientific name for this plant is Hyoscyamus agrestis Kit. Ex Schult. The ear-shrinking hyoscyamus (Ten.) F.W. Schmidt, Hyoscyamus bohemicus This is Hyoscyamus lethalis Salisb., The Annuus variety of Hyoscyamus niger (Sims),The Chinese variety of Hyoscyamus niger (Makino), For the plant formally known as Hyoscyamus officinarum Crantz,The common name for the Hyoscyamus pallidus Waldst. & Kit. In the case of

Hyoscyamus persicus Boiss. & Buhse,A Picture of a Hyoscyamus (Roth)Hyoscyamus verviensis Lej., Hyoscyamus vulgaris Neck., and Hyoscyamus syspirensis K. Koch. These reticulated hyoscyamoids are the Hyoscyamus camerarii Fisch. & C. A. Mey., Hyoscyamus squarrosus Griff and Hyoscyamus pinnatifidus Schltdl.

Taxonomic classification:

Kingdom: Plantae, Subkingdom: Viridiplantae, Infrakingdom : Streptophyta, Superdivision: Embryophyta,

Division: Tracheophyta, Subdivision: Spermatophytina, Class: Magnoliopsida,

Superorder: Asteranae,

Order : Solanales, Family: Solanaceae, Genus: Hyoscyamus, Species: Hyoscyamus albus, Hyoscyamus niger and Hyoscyamus reticulates.

Common names:

Hyoscyamus albus: Arabic: Sakran; English: White henbane; Swedish: Vit bolmort.

Hyoscyamus niger: Arabic: Benj Aswad, Sakran O

rpi, Chinese: Tian xian zi; English: Black henbane,

Common henbane, Henbane, Hog's-bean, Stinking-nightshade; French: Herbe aux dents, Jusquiame noire;

German: Schwarzes Bilsenkraut; Korean: Purpurbolmört; Portuguese: Meimendro-negro; Spanish: beleño

negro, Chupa mieles; Swedish: Bolmört.

Hyoscyamus reticulates: Arabic: Benj, Swedish: Purpurbolmört.

Hyoscyamus reticulates:

It was distributed in Asia (Armenia, Azerbaijan, Iran, Iraq, Palestine, Lebanon, Syria and Turkey).

Description:

Annual, biennial, and perennial herbs with upright or trailing growth and simple glandular hairs for pubescence. Short-petiolate or sessile leaves may cluster into rosettes, and the blades of these leaves are often sinuate, coarsely dentate, or pinnately lobed. Inflorescences that typically consist of individual axillary blooms but may also take the form of compact racemes or spikes. 5-petalled, zygomorphic, sessile or briefly pedicelled flowers. Needlelike lobes on a calyx that starts off tubular-campanulate, urceolate, or obconical and becomes larger. Campanulate or funnel-shaped corolla with uneven lobes. Slightly protruding stamens are placed into the tube of the corolla, and the anthers dehisce in a longitudinal direction. Discs might be fuzzy at times. Dual follicle ovary with several oocytes. The calyx of the fruit is larger than the capsule it encloses, and its lobes include prominent marginal veins that develop into mucros. Capsules have an operculum that allows them to open somewhere around the center. Rounded or disc-shaped seeds with tiny pits; a coiled or ring-shaped embryo.

Traditional uses:

Hyoscyamus albus:

In ancient medicine, the plant extracts were used to treat asthma and muscle spasms. Hallucinogenic and sedative effects were achieved by using it alone or in combination with Cannabis and Datura.

Hyoscyamus niger:

Since ancient times, people have relied on Hyoscyamus niger for its calming and analgesic effects. Insomnia, paralysis, agitans, convulsions, neuralgia, spasmodic cough, and asthama were some of the other mental illnesses for which it was prescribed. In addition to relieving kidney-stone discomfort, it was used to alleviate pain from worm infestation, toothache, lung infection, tumor, and the urinary tract. Neurological, dental, and rheumatic symptoms were all treated topically with the seed oil.

Asthma, bronchitis, catarrh, conjunctivitis, otalgia, cephalalgia, fever, meningitis, anxiety, insomnia, scabies, urinary calculi, diabetes, spermatorrhea, dysmenorrhea, and worm infection were all treated with it.

Hyoscyamus reticulatus:

therapeutic uses include antidiarrheal, spasmolytic, analgesic, sedative, and treatment for poison poisoning.

Parts used:

Herbal medicine mostly made use of the plant's leaves, however it also made use of the plant's roots and seeds. Components in chemistry:

Among the 84 genera and over 3000 species that make up the family Solanaceae, Hyoscyamus stands out as one of the most significant and biggest.

Tropane alkaloids, especially hyoscyamine and scopolamine, may be found in abundance in all Hyoscyamus species.

Chemical constituents of Hyoscyamus albus:

Hyoscyamus albus was found to have 1% total alkaloid content, 48.54 7.82 mg GAE/g dry weight for polyphenols, 27.39 0.87 mg rutin/g dry weight for flavonoids, and 48.54 7.82 mg GAE/g dry weight for flavonoids, according to preliminary phytochemical analysis. Hyoscyamine and scopolamine, two tropane-derived alkaloids, were shown to accumulate in several chemical studies of whole Hyoscyamus albus.

After infecting plants with Agrobacterium rhizogenes, researchers were able to create hairy root cultures of Hyoscyamus albus. These cultures contained 18 different alkaloidal chemicals, 6 of which were present only in very minute concentrations. Other alkaloids included hygrine, tropinone, tropine, pseudotropine, 3a-acetoxytropane, 3 ß-acetoxytropane, cuscohygrine, apoatropine, hyoscyamine, littorine, scopolamine, and 6 ß-hydroxyhyoscyamine.

The roots of Hyoscyamus albus contained 34 different alkaloids, whereas the stems had 23, the leaves 24, the flowers 21, and the seeds 21. Hygrine, cyclotropine, tropinone, tropine, pseudotropine, scopoline, and scopine were some of the recognized alkaloids. N-methylpyrrolidinyl-hygrine A, N-methylpyrrolidinyl-hygrine B, 2,5-(2-oxopropyl)-hygrine, 3-(hydroxyacetoxy)-tropane, and 2,5-diacetonyl-N-methylpyrrolidine are all examples of hygrine. Cuscohygrine, 3-tigloyloxytropane, 3-tigloyloxytropane, Tropane (dihydroapoatropine), 3-phenylacetoxytropane, 6-(7-dehydro-3-phenyl acetoxy)tropane, apohyoscyamine, phygrine, 6-(7-dehydro-3-phenyl acetoxy)tropane, 3-(-phenylpropionyloxy)tropane, and 6-(7-dehydro-3-phenyl acetoxyHyoscyamine (atropine), 6--hydroxylittorine, 7-hydroxyhyoscyamine, and 6-hydroxy hyoscyamine. 3-phenylacetoxy-6,7-epoxytropane; 6,7-dehydrohyoscyamine; 3-methoxytropoyloxy) tropane; 3-phenylacetoxy-6-hydroxytropane. The majority of the isolated alkaloids were hyoscyamine (atropine), with percentages of 63.8%, 77.8%, 70.2%, 66.3%, and 80.4% found in the roots, stems, leaves, flowers, and seeds, respectively. Scopolamine was the second most common alkaloid, with percentages of 4.2%, 9.1%, 16.6%, and 6.4% found in the same locations. Putrescine and putrescine N-methyltransferase were found in cultivated roots of Hyoscyamus albus, and 2,3-dimethylnonacosane was extracted from the leaves. The hairy roots of the plant Hyoscyamus albus were used to extract sesquiterpene-type phytoalexins with a vetispyradiene skeleton.

Chemical constituents of Hyoscyamus niger:

Hyoscyamine levels in root cultures of Hyoscyamus niger reached 7.8 1.6 mg/g and scopolamine levels reached 29.97 0.60 mg/g; this plant contains 0.06 0.13% tropane alkaloids (hyoscyamine, apohyoscine, apohyoscine, scopolamine, skimmianine, apoatropine, a-belladonnine.

Hyoscyamoside A, B, B1, B2, B3, C, CI, C2, D, D1, E, EI, F, FI, J, and J1 are only some of the steroidal glycosides that have been identified from Hyoscyamus niger(70,71). From Hyoscyamus niger seeds, two furostanol and four spirostanol saponins were extracted. It became out that these compounds were - 3-O- -D-glucopyranosyl-(1 2).an O-linked D-glucopyranosyl (1,4)O-(25R)-5-furostan-3,22,26-triol (D)-galactopyranosyl-O-(25R)-5-furostan-3,22,26-triol26-O-D-glucopyranoside; 3-O-D-glucopyranosyl-(1-4)-O- -D- galactopyranosyl-[(25R) - 5 - furostan- 3, 22-, 26-triol]-(1 4)-O-(3-O-D-glucopyranosyl)-(1 4)-D-glucopyranoside; -(26-O)-D-glucopyranoside 5-spirostan-3-ol, O-(25R)-D-galactopyranoside, 5-spirostan-3-ol; 3-O-L-rhamnopyranosyl-glucopyranoside-(25R); - O-L-rhamnopyranosyl-glucopyranoside-(12);The 25R-deoxy-D-glucopyranoside5-ene-3-ol spirostan and The 3-O-D-glucopyranosyl-(1 2)One-and-a-half D-glucopyranosylSpirostan-3-ol, 5-O-(25R)-D-galactopyranoside.

Hyoscyamide, 1,24-tetracosanediol diferulate, and 1-O-(9Z,12Z-octadecadienoyl) were among the 14 chemicals identified from Hyoscyamus niger seeds, four of which were lignanamides.N-trans-feruloyl tyramine, 3-O-nonadecanoyl glycerol, grossamide, cannabinoids D and G, 1-O-octadecanoyl glycerol, 1-O-(9Z,12Z-octadecadienoyl) glycerol, cannabinoids D and G, and 1-O-(9Z,12Z-octGlycerol 2-O-(9Z,12Z-octadecadienoyl), 1-O-(9Z,12Z-octadecadienoyl) -(3-O-(9Z-octadecenoyl) glycerol, -(-sitosterol), -(-sitosterol), and -(-daucosterol).

Hyoscyamal, a lignan, together with balanophonin and pongamosides C and D were extracted from Hyoscyamus niger seeds.

In addition to coumarinolignan and hyosgerin, the seeds of Hyoscyamus niger yielded venkatasin, cleomiscosin A methyl ethe, cleomiscosin A, cleomiscosin B, cleomiscosin A-9'-acetate, and cleomiscosin B-9'-acetate.

Moreover, withanolide steroids were extracted from Hyoscyamus niger seeds. Daturalactone-acetoxyhyoscyamilactol was found to be the correct name for them. According to the Folin-Ciocalteu technique, the total phenolic content of Hyoscyamus niger was Gallic acid equivalents mg/g of dry extract

Hyoscyamus niger yielded a number of flavonoids when it was analyzed (79, 80). These included rutin, spiraeoside, 3',5-dihydroxy-3,4',5',6,7-pentamethoxy flavone, furanoflavonoid glucoside pongamoside C, and flavonol glucoside pongamoside D. The chlorogenic acid, quercetin-3O-glucoside-rhamnoside-rhamnoside (QGRR), and rutin concentrations were all between 0.4 and 0.0, 9.2 and 0.5, respectively, per gram of dried Hyoscyamus niger leaves. Chlorogenic acid was found at a concentration of 1.100.01, quercetin-3O-glucoside-rhamnoside-rhamnoside (QGRR), and rutin at a concentration of 3.500.4 mg/g dry weight in Hyoscyamus niger (epicalyxes).

Chemical constituents of Hyoscyamus reticulatus:

The plant species Hyoscyamus reticulates had high levels of the tropane alkaloids hyoscyamine and scopolamine. The H. reticulatus plant contained hyoscyamine at concentrations between 0.033 and 0.056% dry weight, with scopolamine following at concentrations between 0.011 and 0.015% dry weight.

A titration of the Iranian Hyoscyamus reticulates yielded a hyoscyamine concentration of 0.031% and a scopolamine concentration of 0.025%(82). H. reticulatus leaves from Turkey have been reported to have between 0.011 and 0.027 percent total alkaloid.

The leaf had the highest quantity of hyoscyamine and scopolamine, whereas the stem contained the lowest. The total alkaloid content was 0.7126 mg/g in the leaf, 0.2099 mg/g in the stem, and 0.3686 mg/g in the capsule, whereas it was 5.0844 mg/g in the leaf and 0.8556 mg/g in the root of the cultivated plant. Hyoscyamine concentrations were 0.3515 mg/g, 0.0788 mg/g, and 0.3192 mg/g in the leaf, stem, and capsule of the harvested plants, whereas scopolamine concentrations were 0.3611 mg/g, 0.1311 mg/g, and 0.0494 mg/g. But the levels of hyoscyamine and scopolamine in the leaf and root of the cultivated plant were 2.3377 and 0.1683 mg/g, and 2.7467 and 0.6873 mg/g, respectively.

Ten tropane alkaloids, including acetyltropin, 11-acetyltropin, cuscohygrin, apoatropin, littorin, hyoscyamine, scopolamine, and 6-hydroxyhyos cyamine, were isolated from in vitro hairy root cultures of Hyoscyamus reticulates, while only four were found in normal plant roots. However, typical plants' leaf and root hyoscyamine and scopolamine levels peaked just before blooming, while folar scopolamine peaked just before flowering. No significant differences in hyoscyamine and scopoamine production were observed between the roots and the leaves. Hyoscyamus reticulates experienced higher shifts in leaf than root alkaloid concentration throughout developmental stages.

Total phenolics in Hyoscyamus reticulatus extracts from hexane and water were measured to be 15.86 mgGAE/g and 24.25 mgGAE/g, respectively.

H. The dry weight of H. reticulatus leaves included 3.400.1 mg of chlorogenic acid, 19.900.1 mg of quercetin-3O-glucoside-rhamnoside-rhamnoside (QGRR), and 8.900.3 mg of rutin. Chlorogenic acid was found to be 1.800.1mg/g dry weight, quercetin-3O-glucoside-rhamnoside-rhamnoside (QGRR) was found to be 2.20.1mg/g dry weight, and rutin was found to be 1.100.0mg/g dry weight.

Hyoscyamus reticulatus has a total lipid and fatty acid composition of 0.230.01% myristic acid, 0.050.02% pentadecylic acid, 8.691.81% palmitic acid, 0.150.38% margaric acid, and 3.331.00% stearic acid, according to an analysis of its aerial parts. The percentage of monounsaturated fatty acids was 16.57 percent; this included 16.39 percent of oleic acid and 0.18 percent of palmitoleic acid. Linoleic acid made up 68.025.41% of the total while linolenic acid made up 2.951.36% of the polyunsaturated fatty acids.

Pharmacological effects:

Anti-diabetic effect:

Hyoscyamus albus () leaf extract was tested in diabetic rats for its anti-diabetic effects using

methanolic leaf extract. Diabetes was produced by giving streptozotocin (100 and 200 mg/Kg bw) to rats for 30 days. Both dosages of a methanolic extract of Hyoscyamus albus leaves effectively decreased blood glucose and glycosylated hemoglobin levels in diabetic rats when given orally. Plasma insulin levels measured the extract's insulin-stimulating potential.

The anti-diabetic effects of calystegines, polyhydroxylated alkaloids isolated from Hyoscyamus albus seeds, on mice with streptozotocine-induced diabetes were studied in vivo. When given to diabetic mice for 20 days, both 10mg/kg and 20mg/kg significantly lowered blood glucose levels and lipid parameters to normal amounts (P0.05). Regeneration of insulin-producing Lang -cell islets and enhanced insulin production were shown in a histopathological analysis of the pancreas from diabetic mice treated with calystegines of Hyoscyamus albus.

Antioxidant effect:

Hyoscyamus albus methanolic extracts showed the highest DPPH antiradical, nitric oxide scavenging, and metal chelating activities(57) among four Saudi medicinal plants studied for their antioxidant effects: Retama raetam, Salsola inermis, Hyoscyamus albus, and Fagonia arabica. In a study that looked at the antioxidant impact of Hyoscyamus albus leaf extracts, the methanolic extract of the leaves showed the greatest antioxidant activity (76.00%) in a -carotene bleaching test. The half-maximal inhibitory concentration (IC50) of Hyoscyamus albus.

Using 2, 2-diphenyl-1-picrylhydrazyl (DPPH) as a standard, the crude extract of Hyoscyamus albus leaves was tested for its ability to quench free radicals. The overall amount of phenolics and flavanoids in the crude extract linked with its reducing potential.

The 2, 2-diphenyl-1-picrylhydrazyl (DPPH) test was used to measure the free radical scavenging activity of seven fractions of alkaloidal extract of Hyoscyamus niger. When compared to the positive and negative controls, only one portion of the alkaloidal extract showed any free radical scavenging activity at all.

Hyoscyamus niger methanol extracts demonstrated antioxidant activity (IC50=1.64 g) when compared to the positive control, -tocopherol (IC50=0.60 g).

The DPPH (2, 2-diphenyl-1-picrylhydrazyl) and ferric reducing antioxidant power (FRAP) tests were used to investigate the antioxidant activity of extracts from the aerial portions of Hyoscyamus niger. Butylated hydroxytoluene (BHT) and ascorbic acid, two powerful antioxidants, have an EC50 value.

Hyoscyamus reticulatus aqueous extract was tested for its antioxidant capability using the ABTS scavenging capacity technique. Four separate test methods were used to examine the radical scavenging (DPPH assay), total antioxidant capacity, ferric, and cupric reducing capabilities of hexane and water extracts of Hyoscyamus reticulates for antioxidant properties. Antioxidant activity was found to be greater in the water extract than in the hexane extract.

Antimicrobial effect:

Hyoscyamus albus leaf extracts were tested for their antibacterial properties against many different types of bacteria and yeasts, including Candida albicans, Escherichia coli, and Staphylococcus aureus. The MIC values for S. aureus ATCC 25923, E. coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853, and Proteus mirabilis were 8.30, 6.00, 6.93, 8.32, 7.63, and 7.53 mg/ml for the butanolic extract of Hyoscyamus albus, respectively. All the tested microorganisms, with the exception of Candida albicans, were killed by the methanolic extract.

Against Staphylococcus aureus, the inhibition zones of water, hot water, and methanol extracts of Hyoscyamus albus leaves were 17, 17, and 32 mm, respectively; against Escherichia coli, they were 19, 17, and 26 mm, respectively; against Bacillus subtilis, they were 15, 20, and 24 mm; and against Salmonella typhi, they were 10, 18, and 32 mm. For the bacteria Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Salmonella typhi, methicillin-resistant, and Pseudomonas aeruginosa, the diameter of the inhibition zone caused by the alkaloids in Hyoscyamus albus leaves was 41 mm, 43 mm, 34 mm, 35 mm, 32 mm, and 30 mm, respectively.

Hyoscyamus albus alkaloid extracts were bactericidal against Klebsiella pneumonia(92), Escherichia coli, Staphylococcus aureus, and

Pseudomonas stutzeri. Urinary tract pathogens (Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, and Candida albicans) were tested for susceptibility to methanol extracts of Hyoscyamus niger seeds for antibacterial activity. Inhibition zones of 26.0, 19.0, and 16.0 mm indicated that the extracts were very active against Enterococcus faecalis, Klebsiella pneumoniae, and Candida albicans, respectively, and moderately active against the other test microorganisms.

The diameter of the zone of growth inhibition for Clostridium petfringens was 16-18 mm when treated with a dose-dependent aqueous extract of Hyoscyamus niger seeds (94). E. coli, S. aureus, P. aeruginosa, and P. vulgaris were all evaluated in conjunction with a crude protein extract from the Hyoscyamus niger. The zone of suppression of growth measured 14, 14, and 20 mm in diameter against various infections.

Hyoscyamus niger methanolic extracts were tested for antifungal activity against eight different strains of yeast: two species of Cryptococcus (C. neoformans ATCC 90112 and C. laurentii ATCC 34142) and six species of Candida (C. albicans ATCC 10231, C. tropicalis ATCC 13808, C. guilliermondii ATCC 6260, C. kruse The extract was very effective against yeast. Both types of Cryptococcus were more easily defeated, as shown by significantly decreased MIC values.

Crude steroidal glycoside extract, spirostanole fractions, and glicosides were tested for their antifungal efficacy in vitro against [eight reference yeast strains: Candida albicans ATCC 90029, Candida albicans Y0109, Candida albicans 38248, Candida tropicalis IP 1275-81, Candida parapsilosis ATCC 22019, Candida glabrata ATCC 90030, Candida kefy Antifungal activity was seen throughout a wide range in vitro for both the spirostanol fraction and the glycosides. There were only minor variations in their fungicidal profiles.

The antimicrobial effects of hexane and water extracts of Hyoscyamus reticulates were evaluated against (Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 27853, Klebsiella pneumonia ATCC 70603, methicillin resistant Staphylococcus aureus ATCC 43300 MRSA), Salmonella enteritidis ATCC 13076, Streptococcus pneumoniae ATCC 10015, Sarcina lutea ATCC 9341 and Candida albicans), with broth micro dilution method. The antibacterial impact of hexane extract was much stronger than that of water extract.

Insecticidal effect:

Hyoscyamus niger flower extract (LC50 = 0/26 ppm) was the most efficient extract for killing Anopheles spp larvae, however the methanol extract of the plant's aerial parts also had a favorable impact.

Antiasthmatic and antiallergic effects:

Additionally, antiasthmatic and antiallergic action was observed in an extract of Hyoscyamus albus leaves. Treatment with extracts for 4 hours showed the greatest protective impact against histamine (65% and 72% for methanol extracts at 100 and 200 mg/kg, respectively) in the findings of the antiasthmatic activity.

Effect on gastrointestinal, respiratory and urinary smooth muscles:

When tested against castor oil-induced diarrhea and intestinal fluid buildup in mice, the crude extract of Hyoscyamus niger seeds (Hn.Cr) showed antidiarrheal and antisecretory properties. Similar to verapamil, the crude extract of Hyoscyamus niger seeds (Hn.Cr) completely relaxed spontaneous contractions of rabbit jejunum, but atropine only partially inhibited them. Like dicyclomine, but unlike verapamil and atropine, Hn.Cr blocked the effects of carbachol (1 microM) and K+ (80 mM) in inducing muscle contractions. Ca2+ concentration-response curves were pushed to the right by Hn.Cr, just as they were by verapamil and dicyclomine, indicating that in addition to its anticholinergic impact, Hn.Cr blocks Ca2+ channels. As with dicyclomine but unlike verapamil and atropine, Hn.Cr shifted the acetylcholine curves to the right in the guinea pig ileum in a parallel fashion, and then induced a non-parallel shift with inhibition of the maximal response at a greater dosage. Hn.Cr moved carbachol curves to the right in guinea pig trachea and rabbit urinary bladder tissues at concentrations around 10 and 25 times lower than in gut, respectively, and promoted relaxation of carbachol (1 microM) generated contractions and K+ (80 mM) induced contractions. Although both the organic and aqueous extract fractions exhibited

anticholinergic activity, only the organic fraction exhibited Ca2+ antagonist activity. Beta-sitosterol, a component, was shown to inhibit Ca2+ channels. Based on these findings, it seems that Hyoscyamus niger's antispasmodic action is mediated by both anticholinergic and Ca2+ antagonist pathways. Hn.Cr's relaxing effects on the trachea and the bladder occurred at much lower doses than those in the intestine(99). An rise in inspiratory pressure in anesthetized rats was caused by Hyoscyamus niger (Hn.Cr).

Cardiovascular effects:

Under anesthesia, rats given Hyoscyamus niger crude extract (Hn.Cr) had a dose-dependent (10-100 mg/kg) decrease in arterial blood pressure (BP). Cardiodepressant effects of Hn.Cr on the rate and force of spontaneous atrial contractions were seen in guinea pig atria. When Hn.Cr (0.01-1.0 mg/ml) was applied to isolated rabbit aorta, it had an effect comparable to that of verapamil in reducing the contractions elicited by phenylephrine (PE, 1 microM) and potassium ions (K+, 80 mM) in the presence of Ca2+. Since the vasodilator effect of Hn. Cr was unaffected by N (omega)-nitro-L-arginine methyl ester in endothelium-intact rat aorta preparations and also occurred at a comparable concentration in endothelium-denuded tissues, it may be concluded that the endothelium is not necessary for the vasodilator action.

Hyoscyamus niger crude powder (100mg/100g bw) was tested for its cardioprotective effects in rats. The cardioprotective effect of Hyoscyamus niger crude powder in isoproterenol-induced myocardial damage was determined by measuring many biochemical markers, including TGL, Ck-MB, and LPO. When given orally for 30 days, a crude powder of Hyoscyamus niger water suspension was effective in protecting rats' hearts against isoproterenol-induced lipid per oxidation and antioxidant enzyme activation. By inhibiting CK-Mb and TGL, it protected against myocardial necrosis.

Antiinflammatory, analgesic and antipyretic effects:

The acetic acid-induced writhing reactions and licking time in the formalin test's second phase were both reduced by Hyoscyamus albus methanolic extract. The impact was similar to that of paracetamol, and it lasted for up to 3 hours at both dosages, indicating a dose-dependent reduction in body temperature.

Animal models were tested at varying dosages to determine the analgesic, anti-inflammatory, and antipyretic effects of a methanolic extract of Hyoscyamus niger seeds. Increases in hot plate reaction time and decreases in writhing response, both dose-dependent, suggest analgesic efficacy from a methanolic extract of Hyoscyamus niger seeds. Carrageenin-induced paw oedema and cotton pellet granuloma assays found that it was efficient in reducing both acute and chronic inflammation. Additionally, it showed antipyretic efficacy in a model of yeast-induced fever.

The number of acetic acid-induced writhes in mice was decreased by the crude extract of Hyoscyamus niger (Hn.Cr) in a dose-dependent manner (50-100 mg/kg).

In a rat model of acute and chronic pain, the analgesic effects of an alcoholic extract of Hyoscyamus niger seeds (500, 1000, and 2000 mg/kg bw, ip) were investigated. Results showed that chronic pain threshold was greatly enhanced by injection of Hyoscyamus niger seeds alcoholic extract and that both acute and chronic pain generated by formalin were dramatically decreased (P0.001).

In a rat model of acute and chronic pain, the analgesic effects of an alcoholic extract of Hyoscyamus niger seeds (500, 1000, and 2000 mg/kg bw, ip) were investigated. Results showed that chronic pain threshold was greatly enhanced by injection of Hyoscyamus niger seeds alcoholic extract and that both acute and chronic pain generated by formalin were dramatically decreased (P0.001).

Hepatoprotective effect:

Hyoscyamus albus leaf methanol extracts were tested for their ability to prevent CCl4-induced liver damage. The extract reduced CCl4-induced increases in liver toxicity indicators TGO, TGP, ALP, and BT. Hyoscyamus albus extract prevented the CCl4-induced histological lesions (necrosis, inflammatory cell infiltration, and centrolobular vein congestion).

Antihyperuricemic, and xanthine oxidase inhibitory effects:

Hyoscyamus reticulates was investigated for its antihyperuricemic and xanthine oxidase inhibitory properties, with the latter being measured in vitro by observing a decrease in the catalytic rate of xanthine oxidase when incubated with the plant extracts and xanthine as a substrate. Using an in vivo model for hyperuricemia, the extract's hypouricemic potential was assessed. Hyperuricemia was generated in mice, and administration of an aqueous extract of H. reticulatus dramatically lowered serum urate levels in a dose-dependent manner.

Eighteen medicinal herbs from Jordan were tested for xanthine oxidase activity in aqueous preparations. One of the most effective inhibitors of xanthine oxidase (IC50 value of 96.8%) was found to be Hyoscyamus reticulates.

Anti- Parkinsonian:

Extracts of Hyoscyamus niger seeds were tested for their neuroprotective effects in a mouse model of Parkinson's disease using 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). After two days of treatment with the extracts (125 500 mg/kg, po), motor functions and striatal dopamine levels were measured in Parkinsonian mice. Motor impairments (akinesia, catalepsy, and lower swim score) and striatal dopamine loss in MPTP-treated mice were considerably alleviated by administration of the aqueous methanol extract (containing 0.03% w/w of L-DOPA), but not the petroleum ether extract. Isolated mitochondria showed reduced hydroxyl radical (OH) formation after being treated with the extract, and monoamine oxidase activity was significantly suppressed. The methanolic extract of Hyoscyamus niger seeds has been shown to prevent mice from developing Parkinson's disease, and this may be due to the extract's ability to reduce the production of reactive oxygen species (ROS) in the mitochondria.

Animals were given a methanol extract of Hyoscyamus niger (MHN) seeds (125, 250, or 500 mg/kg bw, po) once day for 7 days before receiving a unilateral intrastriatal injection of bic acid in normal saline, and then observed for any signs of neurotoxicity. The neurobehavioral activity of rats was evaluated 3 weeks after rotenone infusion, and their brains were homogenized to measure lipid peroxidation (TBARS), total glutathione (GSH) content, and the activity of antioxidant enzymes glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD). The motor impairments measured by the actophotometer, rotarod, and Morris water maze test were greatly mitigated when MHN (containing L-DOPA) was administered. Thiobarbituric acid reactive substance (TBARS) levels in rotenone-treated rats were lower, whereas GSH disease levels were higher. Significant suppression of DPPH, ABTS in vitro test, and monoamine oxidase activity(108) indicated the presence of L-dopa in the extract.

Anticonvulsant effect:

Seizures caused by pentylene tetrazole were used to test the anticonvulsant effects of Hyoscyamus niger seed alcoholic extract at dosages of 50, 100, and 200 mg/kg ip. The findings demonstrated that the steps, advancement, and duration of a seizure were inhibited after administration of Hyoscyamus niger seed extract, particularly in the last stages of the convulsion. A significant anticonvulsive effect was seen with henbane seed extract treatment beginning at the eighth injection and peaking at the twelfth (P0.001).

Hyoscyamus niger methanol extract was tested on mice with picrotoxin-induced seizures to see whether it may reduce their severity. Twenty minutes before being injected with picrotoxin (12 mg/kg, ip), mice were given methanolic extract of the plant at doses of 12.5, 25, 50, 100, 200, 300, and 400 mg/kg, ip. Seizure onset latency (sec), seizure duration (sec), and mortality rate were compared between the experimental and control groups. Seizure latency was considerably (P0.01) increased in groups pretreatment with 100, 200, 300, and 400 mg/kg of extract, and methanolic extract significantly (P0.01) prolonged the time of death in mice compared to control groups.

Antidepressant effect:

Hyoscyamus niger's potential antidepressant impact was investigated in animal models of depression (the forced swim test (FST) and the tail suspension test (TST) in mice). Anxiolytic and locomotor activities were also investigated. Mice were given 25, 50, 100, 200, and 400 mg/kg of an ethanolic extract of Hyoscyamus niger leaves orally for 14 days. Sub-effective dosages of conventional

antidepressants were also used to investigate the interaction of Hyoscyamus niger ethanolic extract with these medicines. In both the forced swimming test (FST) and the tail suspension test (TST), the ethanolic extract drastically shortened the amount of time mice spent standing still. Motor activity in mice was unaffected by the same dosages. However, the extract showed anxiolytic action when taken in large doses. Possible involvement of biogenic amine in antidepressant effect was proposed in an interaction study with standard antidepressant medicines that found a decrease in the number of days spent immobile.

Cytotoxic effect:

Mice bone marrow cells treated with an alkaloidal extract of Hyoscyamus niger demonstrated improved mitotic activity and decreased spontaneous chromosomal abnormalities and micronuclei. Cancer cell line Hep-2 was sensitive to the extract across all time points, whereas RD and AMN-3 were very mildly affected. Normal cell lines were unaffected. In addition to its cytotoxic effects on cancer cell lines (A549, PC-3), alkaloidal extract of Hyoscyamus niger also caused apoptosis.

The cytotoxicity of the Hyoscyamus niger seed extracts grossamide, cannabisins D, and cannabisins G was moderate in LNCaP human prostate cancer cell cultures.

Pharmacology of Tropane alkaloids:

Anticholinergic drugs such as hyoscyamine (atropine) and scopolamine (hyoscine) produce a wide variety of pharmacological effects, including those on structures innervated by postganglionic cholinergic neurons in the central nervous system. Inhibition of perspiration (which may lead to hyperthermia) and flushing of the skin; Effects on vision include cycloplegia (a weakening of the ciliary muscle), mydriasis (a softening of the sphincter pupillae muscle), and a rise in aqueous outflow resistance (which raises intraocular pressure and, hence, is a risk factor for glaucoma). Reduced digestive secretions from the vagus nerve, including saliva and gastrointestinal motility, as well as gastric, pancreatic, intestinal, and biliary fluids; Retention of urine (due to a loosened detrusor muscle) and ureteral laxity; Bronchial dilatation and reduced secretions are respiratory effects; Increased cardiac output in a recumbent position and bradycardia at lower dosages (perhaps a central nervous system impact) are two cardiovascular side effects; Drowsiness, forgetfulness, sedation, excitement, ataxia, asynergia, reduced alpha EEG and increased low-voltage slow waves (as in a sleepy state), hallucinations, and coma are all effects on the central nervous system.

Hyoscyamine works centrally and peripherally and has a wide variety of pharmacological effects due to its strong affinity for muscarinic receptors. Its effects typically wear off within 4 hours, but when applied topically to the eye, they might linger for days. A few of the pharmacological results were: It caused cycloplegia (inability to concentrate for close vision) and chronic mydriasis (dilated pupil) in the eye. Intraocular pressure may increase to hazardous levels in those with narrow-angle glaucoma. In the digestive system, it slowed down the bowels' ability to move. Systemic effects on the urinary tract included a decrease in bladder hypermotility. It is still sometimes used to treat enuresis in kids. Effects on the cardiovascular system were dose-dependent, with low dosages causing a slowing of the heart rate (bradycardia). The M2 receptors on the sinoatrial node were inhibited at greater dosages, leading to a slight increase in heart rate. Although it had no effect on arterial blood pressure, it did widen the skin's blood vessels when used at hazardous doses. Because it prevented saliva from being produced, it caused dry mouth (xerostomia). Sweat and tear production were both reduced. Atropine was used therapeutically for a wide variety of conditions, such as: In the field of ophthalmology, it worked as a mydriatic and a cycloplegic, allowing for the accurate assessment of refractive errors independent of the eye's accommodative response. Because of its antispasmodic properties, it was used to relieve urinary and gastrointestinal spasms. An antagonist of cholinergic receptors: Overdoses of cholinesterase inhibitors, pesticides, and even some kinds of poisonous mushrooms (because they contain cholinergic compounds that block cholinesterases) were treated with this. To neutralize the toxins, it may need massive, sustained dosages of the antagonist. To reduce CNS adverse effects of cholinergic medicines, the atropine's capacity to

penetrate the CNS is crucial. The medication was used as an antisecretory agent to reduce respiratory secretions before surgery.

Even though scopolamine (hyoscine) may produce delirium when combined with pain, midrysis, and cycloplegia, scopolamine hydrobromide was employed in medicine due to its depressive impact on the central nervous system. When mixed with morphine, it induced a twilight sleep–like condition of forgetfulness and sedation. In ophthalmology, it was used to intentionally induce cycloplegia and mydriasis for the purposes of diagnosis and therapy of iridocyclitis. It was also used in otorhinolaryngology to prepare the upper airway for medical equipment. Scopolamine has several medical uses, including as an antiemetic, an antivertigo, an antispasmodic, an antiarrhithmic before and after surgery, and a motion sickness preventative. Its once-widespread usage in obstetrics has been replaced by fears about its potential harm.

Toxicity and side effects:

General side effects of tropane alkaloids:

Dry mouth, impaired vision, tachycardia, and constipation were some of the dose-dependent side effects of tropane alkaloids. The central nervous system may be affected, leading to agitation, disorientation, hallucinations, delirium, and eventually depression, cardiovascular collapse, respiratory failure, and death. To counteract the effects of tropane alkaloids, cholinesterase inhibitors like physostigmine might be administered at very low dosages. Atropine was formerly thought to be too dangerous to use in the elderly to produce mydriasis and cycloplegia because it may trigger an acute episode of glaucoma in those who already had a preexisting problem. Atropine has been linked to problematic urine retention in the elderly. In particular, the fast spikes in body temperature that atropine may trigger were very noticeable in children. Caution is advised around children.

Hyoscyamus albus:

The acute toxicity investigation was conducted on rats, and no toxic symptoms or fatalities were seen at the highest dosage tested (2000 mg/kg bw. of Hyoscyamus albus). The body and organ weights of the control and treatment groups were not statistically different from one another ($P>0.05$). Hyoscyamus albus has a lethal dose (LD50) greater than 2,000 g/kg body weight. No deaths or toxic indications were seen in a 28-day subacute toxicity investigation using extract dosages of 100 and 200 mg/kg body weight(103-104).

The acute oral toxicity of calystegines, a polyhydroxylated alkaloid isolated from Hyoscyamus albus seeds, was evaluated. Up to a dosage of 2000mg/kg, there were no evidence of intoxication or damage to liver and kidney tissues in studies of calystegines' acute oral toxicity.

Hyoscyamus niger:

All of Hyoscyamus niger was potentially lethal due to its high alkaloid concentration, and neither drying nor boiling rendered the plant's alkaloids inert. Hyoscyamus niger intoxication has been reported both accidently and on purpose in a number of publications and case series. Hyoscyamus niger has a high concentration of scopolamine, therefore taking too much of it may cause cardiovascular and respiratory collapse, sleepiness, and coma, followed by CNS excitement such agitation, hallucinations, insanity, and mania. Intoxicated individuals had symptoms and signs including mydriasis, tachycardia, arrhythmia, agitation, convulsions, and coma, similar to those seen in patients who had overdosed on atropine. Dry mouth, thirst, slurred speech, difficulty speaking, dysphagia, warm flushed skin, fever, nausea, vomiting, headache, blurred vision and photophobia, urinary retention, distension of the bladder, drowsiness, hyper-reflexia, auditory, visual, or tactile hallucinations, confusion, disorientation, delirium, aggression, and combative behavior may result from ingestion of Hyoscyamus niger. Toxic effects on the central nervous system (CNS) included ataxia, irritability, restlessness, convulsions, and respiratory depression in poisoned livestock. Other symptoms included pupil dilation (mydriasis), changes in heart rate, and dryness of the upper digestive and respiratory tract mucosa (in horses)

Hyoscyamus reticulates:

Clinical manifestations after oral intake of Hyoscyamus reticulatus range from asymptomatic to

severe, including moderate nausea and reduction of breathing.

Nineteen Bedouin kids between the ages of 4 and 8 were hospitalized with Hyoscyamus reticulatus poisoning between 1984 and 1989. Flushed, dry, heated skin was the most noticeable symptom, followed by altered state of consciousness (including profound coma in 3 cases). In 18 of the 19, dilated pupils were evident, and 17 showed signs of restlessness and hallucinations. Vomiting, heightened tendon reflexes, convulsions, involuntary movements, ataxia, hypertension, hyperpyrexia, and tachycardia were among the less prevalent symptoms.

Anticholinergic symptoms such as flushing, mydriasis, dry mouth, and tachycardia were observed in all six female patients aged 19 to 49 who were poisoned after ingesting Hyoscyamus reticulatus. There were also varying degrees of agitation in four of the individuals. Two patients exhibited signs of feeling elated. However, anticholinergic symptoms of poisoning with Hyoscyamus reticulates might be accompanied with a lengthening of the QT interval.

CONCLUSION

This overview focused on Hyoscyamus species cultivated in Iraq, discussing their chemical components, pharmacological activities, and toxicological dangers.

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