IOSR Journal Of Pharmacy www.iosrphr.org
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 8, Issue 6 Version. I (June 2018), PP. 18-32

Therapeutic importance of Hyoscyamus species grown in Iraq (Hyoscyamus albus, Hyoscyamus niger and Hyoscyamus reticulates)- A review

Prof Dr Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, University of Thi qar, Iraq.
Corresponding Author: Prof Dr Ali Esmail Al-Snafi

Abstract: *Hyoscyamus* is one of the most important and largest genera of the family Solanaceae comprising about 84 genera and more than 3000 species. All Hyoscyamus species are rich sources of tropane alkaloids, mainly hyoscyamine and scopolamine. The phytochemical analysis showed that *Hyoscyamus* species contained alkaloids, flavonoids, tannins, terpenes, saponins, carbohydrates, cardiac glycosides and anthraquinones. They exerted many pharmacological effects included anti-diabetic, antioxidant, anticancer, insecticidal, antiasthmatic, antiallergic, antidiarrhoeal, antisecretory, Ca^{2+} channel-blocking, hypotensive, cardioprotective, hepatoprotective, antihyperuricemic, Anti- Parkinsonian, anticonvulsant, antidepressant, in addition to anticholinergic effects of tropane alkaloids. The current review discussed the chemical constituents, pharmacological and toxicological effects of *Hyoscyamus* species grown in Iraq.

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

---

Date of Submission: 28-05-2018 Date of acceptance: 11-06-2018

I. INTRODUCTION:

Herbal medicine is the oldest form of healthcare known to mankind. Herbs had been used by all cultures throughout history. The World Health Organization (WHO) estimates that 80 percent of the world population, presently use herbal medicine for some aspect of primary health care. However, plants are still provide some of our most valuable medicines[1-30]. The phytochemical analysis showed that *Hyoscyamus* species contained alkaloids, flavonoids, tannins, terpenes, saponins, carbohydrates, cardiac glycosides and anthraquinones. They exerted many pharmacological effects included anti-diabetic, antioxidant, anticancer, insecticidal, antiasthmatic, antiallergic, antidiarrhoeal, antisecretory, Ca^{2+} channel-blocking, hypotensive, cardioprotective, hepatoprotective, antihyperuricemic, Anti- Parkinsonian, anticonvulsant, antidepressant, in addition to anticholinergic effects of tropane alkaloids. The current review was designed to highlight the chemical constituents, pharmacological and toxicological effects of *Hyoscyamus* species grown in Iraq.

Plant profile:
Synonyms:
Hyoscyamus albus*: *Hyoscyamus canariensis Ker Gawl., ***Hyoscyamus clusii*** G. Don, Hyoscyamus ***luridus*** Salisb., ***Hyoscyamus major*** Mill., *Hyoscyamus minor* Mill and ***Hyoscyamus varians*** Vis.
Hyoscarpus niger: ***Hyoscarpus niger*** Dulac, ***Hyoscyamus agrestis*** Kit. ex Schult., ***Hyoscyamus auriculatus*** Ten., ***Hyoscyamus bohemicus*** F.W. Schmidt, ***Hyoscyamus lethalis*** Salisb., ***Hyoscyamus niger*** var. ***annuus*** Sims, ***Hyoscyamus niger*** var. ***chinensis*** Makino, ***Hyoscyamus officinarum*** Crantz, ***Hyoscyamus pallidus*** Waldst. & Kit. ex Willdenow, ***Hyoscyamus persicus*** Boiss. & Buhse, ***Hyoscyamus pictus*** Roth, ***Hyoscyamus syspirensis*** K. Koch, ***Hyoscyamus verviensis*** Lej. and ***Hyoscyamus vulgaris*** Neck.
***Hyoscyamus reticulates*:** *Hyoscyamus camerarii* Fisch. & C. A. Mey., *Hyoscyamus pinnatifidus* Schltdl. and *Hyoscyamus squarrosus* Griff[31-33].
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*[34-35].

Common names[36-38]**:**

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

***Hyoscyamus niger*: Arabic:** Benj Aswad, Sakran Orpi**, 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**.**

Distribution[36-38]**.:**

***Hyoscyamus albus*:**

It was distributed in **Africa**: (Algeria, Egypt, Libya**,** Morocco, Tunisia); **Asia**: (Saudi Arabia, Iraq, Palestine, Palestine, Jordan, Lebanon, Syria, Turkey) and **Europe**: (Ukraine, Albania**,** Bulgaria**,** Croatia**,** Greece**,** Italy**,** Romania**,** Slovenia**,** France, Portugal**,** Spain)**.**

***Hyoscyamus niger*:**

It was distributed in **Africa:** (Algeria, Morocco, Tunisia); **Asia:** (Armenia, Azerbaijan, Georgia, Russian Federation, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, China, Japan Afghanistan, Iran, Iraq, Lebanon, Turkey, India, Nepal, Pakistan), **Europe**: (Belarus, Estonia, Latvia, Lithuania, Moldova, Russian Federation, Ukraine, Austria, Belgium; Czech Republic, Germany, Hungary, Netherlands, Poland, Slovakia, Switzerland, Denmark, Ireland, Sweden, United Kingdom, Albania, Bulgaria, Croatia, Greece, Italy, Malta, Romania, Serbia, Slovenia, France, Portugal, Spain) and **Northern America** (United States).

***Hyoscyamus reticulates*:**

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

Description:

Herbs annual, biennial, or perennial, erect or sprawling; pubescence of simple glandular hairs. Leaves sometimes forming a rosette, short petiolate or sessile; leaf blade sinuate, coarsely dentate or pinnately lobed, rarely entire. Inflorescences of solitary axillary flowers, sometimes condensed into scorpioid racemes or spikes. Flowers 5-merous, zygomorphic, sessile or short pedicellate. Calyx tubular-campanulate, urceolate, or obconical, becoming enlarged, lobes erect or spreading, needlelike. Corolla campanulate or funnelform, lobes unequal. Stamens inserted in corolla tube, usually slightly exserted; anthers dehiscing longitudinally. Disc sometimes indistinct. Ovary 2-locular; ovules numerous. Fruiting calyx enveloping and longer than capsule, lobes with strong marginal veins produced into mucros. Capsules dehiscent by an operculum slightly distal to middle. Seeds reniform or discoid, minutely pitted; embryo ringlike or coiled[39-40].

Traditional uses:

***Hyoscyamus albus*:**

The plant extracts were used in traditional medicine as an antiasthmatic and antispasmodic. It was also used as hallucinogenic and sedative alone or mixed with *Cannabis* and *Datura*[41-42].

***Hyoscyamus niger*:**

Hyoscyamus niger has a very long history of use as a medicinal herb, it was used extensively as a sedative and pain killer[43].

It was also used in mental disorders, epileptic mania, and chronic dementia with insomnia, paralysis, agitans, convulsions, neuralgia, spasmodic cough and asthama[44].

It was also used for the treatment of abdominal colic, pain due to worm infestation, toothache, pain of pulmonary infections, tumors pain, pain associated with urinary tract, especially kidney-stone. The seed oil was used externally for neuralgic, dental and rheumatic pains[45-49]

It was also used in odontalgia, bleeding gums, dental caries, mamillitis, orchitis, rheumatoid arthritis, worm infection, colic, dyspepsia, flatulence, cardiac debility, epistaxis, haematemesis, haemoptysis, whooping cough, asthma, bronchitis, catarrh, conjunctivitis, otalgia, cephalalgia, fever, meningitis, anxiety, insomnia, scabies, urinary calculi, diabetes, spermatorrhoea, dysmenorrhoea, leucorrhoea, amenorrhoea, neuralgia, beneficial in irritable affections and urinary tract[50].

***Hyoscyamus reticulatus*:**

It was used in asthma, gastric ulcers, for motion sickness and in Parkinson's disease. It was also used as mydriatic, spasmolytic, analgesic, sedative and as antidote for intoxications of many poisons[51-52].

Parts used:

The leaves were mainly used in herbal medicine, but, roots the seeds were also used [42, 53].

Chemical constituents:

Hyoscyamus is one of the most important and largest genera of the family Solanaceae comprising about 84 genera and more than 3000 species[54]. All Hyoscyamus species are rich sources of tropane alkaloids, mainly hyoscyamine and scopolamine[55].

Chemical constituents of *Hyoscyamus albus*:

The preliminary phytochemical analysis showed that *Hyoscyamus albus* contained alkaloids, flavonoids, tannins, terpenes, saponins, carbohydrates, cardiac glycosides

and anthraquinones, total polyphenols content was 48.54 ± 7.82 mg GAE/g dry weight, total flavonoids content was 27.39 ± 0.87 mg rutin/g dry weight, and total alkaloid content was 1%[56-57].

However, with the using of different extracts, in chloroform extract *of Hyoscyamus albus* leaves, total phenolic, flavonoid and condensed tannins were 99.45 ± 2.75, 18.23 ± 0.78 and 20.38± 0.69 µg EAG/mg of extract, in methanol extract 111 .1 ± 1.82, 24.31 ± 0.62 and 24.87 ± 1.57 µg EAG/mg of extract, and in petroleum ether extract 23.83± 0.21, 6.77± 1.24 and 13.27± 0.69 µg EAG/mg of extract respectively[58].

Many chemical works on intact *Hyoscyamus albus* showed that it accumulated a number of tropane-derived alkaloids, mainly hyoscyamine and scopolamine[59-61].

Eighteen alkaloidal compounds were detected, in hairy root cultures of *Hyoscyamus albus* obtained by an infection of plants with *Agrobacterium rhizogenes*, six of the compounds were in trace amounts. However, some of these alkaloids were hygrine, tropinone, tropine, pseudotropine, 3a-acetoxytropane, 3 ß-acetoxytropane, cuscohygrine, apoatropine, hyoscyamine, littorine, scopolamine and 6 ß-hydroxyhyoscyamine[62].

Thirty-four alkaloids were identified in the roots of *Hyoscyamus albus*, 23 in the stems, 24 in the leaves, 24 for the flowers and 21 in the seeds. The identified alkaloids included: hygrine, cyclotropine, tropinone, tropine, pseudotropine, scopoline, scopine, 2,5-(2-oxopropyl)-hygrine (2,5-diacetonyl-*N*-methylpyrrolidine), 3-(hydroxyacetoxy) tropane, *N*-methylpyrrolidinyl-hygrine A, *N*-methylpyrrolidinyl-hygrine B, 3*α*-tigloyloxytropane, cuscohygrine, 3*β*-tigloyloxytropane, 6,7-dehydro-3-phenyl acetoxytropane, 3-phenylacetoxy tropane, 3-(2'-phenylpropionyloxy) tropane (dihydroapoatropine), 6,7-dehydro-3-apotropoyloxytropane, apohyoscyamine, phygrine, 3-phenylacetoxy-6,7-epoxytropane, 6,7-dehydrohyoscyamine, 3-(3'-methoxy tropoyloxy) tropane, 3-phenylacetoxy-6-hydroxytropane, aponor scopolamine, aposcopolamine, *N*-methylpyrrolidinyl-cuscohygrine A, *N*-methyl pyrrolidinyl-cuscohygrine B, hyoscyamine (atropine), 6-hydroxyapo hyoscyamine, scopolamine, 4'-hydroxylittorine, 7-hydroxyhyoscyamine and 6-hydroxy hyoscyamine. Hyoscyamine (atropine) was the major isolated alkaloid, represented 63.8, 77.8, 70.2, 66.3 and 80.4% of the alkaloids isolated from the roots, stems, leaves, flowers and seeds respectively, followed by scopolamine which represented 4.2, 9.1, 16.6, 16.5 and 6.4% of the alkaloids isolated from the same parts respectively[41].

2,3-dimethylnonacosane was also isolated from the leaves and stems of *Hyoscyamus albus* [33]. Putrescine and putrescine N-methyltransferase were identified in the cultured roots of *Hyoscyamus albus* [64-66].

Sesquiterpene-type phytoalexins with a vetispyradiene skeleton were isolated from *Hyoscyamus albus* hairy roots[67].

Chemical constituents of *Hyoscyamus niger*:

It contained 0.06–0.13% tropane alkaloids (hyoscyamine, apohyoscine, apohyoscine, scopolamine, skimmianine, apoatropine, a-belladonnine, b-belladonnine, tropine)[68], Hyoscyamine reached 7.8 ± 1.6 mg/g and scopolamine 29.97 ± 0.60 mg/g in root cultures of *Hyoscyamus niger* [69].

Many steroidal glycosides, hyoscyamoside A, B, B1, B2. B3, C, CI, C2, D, D1 E, EI, F, FI, J and J1, were isolated from *Hyoscyamus niger*[70-71].

Two furostanol and four spirostanol saponins were isolated from the seeds of *Hyoscyamus niger*. They were identified as - 3-*O*- β-D-glucopyranosyl-(1→2)-*O*-β-D-glucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-[(25*R*)-5α- furostan- 3β, 22α, 26-triol]- 26-*O*-β-D-glucopyranoside; - 3-*O*-β-D-glucopyranosyl -(1→4)-*O*-β-D-galactopyranosyl-[(25*R*) - 5α- furostan- 3β, 22α, 26-triol]-26-*O*-β-D-glucopyranoside; - 3-*O*-β-D-glucopyranosyl -(1→4) -*O*-β-Dgalactopyranoside-(25*R*) - 5α- spirostan - 3β-ol, -3-*O*-α-Lrhamnopyranosyl-(1→2) - β - D-glucopyranoside-(25*R*) - 5α- spirostan - 3β-ol; - *O*-α-L-rhamnopyranosyl- (1→2) - β - D-glucopyranoside -(25*R*)- 5-ene -spirostan -3β-ol and -3-*O*-β-D-glucopyranosyl-(1→2)- β-D-glucopyranosyl -(1→4)-*O*-β-D-galactopyranoside-(25*R*) - 5α- spirostan - 3β-ol[72-73].

Four lignanamides and 10 other nonalkaloidal components were isolated from the seeds of *Hyoscyamus niger*, these compounds inclused hyoscyamide, 1,24-tetracosanediol diferulate, and 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-3-*O*-nonadecanoyl glycerol, grossamide, cannabisin D, cannabisin G, *N*-*trans*-feruloyl tyramine, 1-*O*-octadecanoyl glycerol, 1-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol, 1-*O*-(9*Z*,12*Z*-octadecadienoyl)-2-*O*-(9*Z*,12*Z*-octadecadienoyl) glycerol, 1-*O*-(9*Z*,12*Z*-octadecadienoyl) -3-*O*-(9*Z*-octadecenoyl) glycerol, rutin, vanillic acid, β-sitosterol, and daucosterol[74].

A lignan, hyoscyamal, and three other compounds, balanophonin, pongamoside C and pongamoside D were isolated from the seeds of *Hyoscyamus niger* [75].

Coumarinolignan, hyosgerin, venkatasin, cleomiscosin A methyl ethe, cleomiscosin A, cleomiscosin B, cleomiscosin A-9'-acetate and cleomiscosin B-9'-acetate, were also isolated from the seeds of *Hyoscyamus niger* [76-77].

In addition, withanolide steroids were isolated from the seeds of *Hyoscyamus niger*. They were identified as daturalactone-4 and hyoscyamilactol and 16α-acetoxyhyoscyamilactol[78].

The total phenolic content of *Hyoscyamus niger* as determined by Folin-Ciocalteu method, was 5833.33±0.4 Gallic acid equivalents mg/g of dry extract[45]

Flavonoids like rutin, spiraeoside, 3',5-dihydroxy-3,4',5',6,7-pentamethoxy flavone; furanoflavonoid glucoside, pongamoside C and flavonol glucoside, pongamoside D were isolated from *Hyoscyamus niger* [79-80].

Hyoscyamus niger (leaves) contained chlorogenic acid 0.4±0.0, quercetin-3*O*-glucoside-rhamnoside-rhamnoside (QGRR) 0.4±0.0 and rutin 9.2±0.5 mg/g dry weight. *Hyoscyamus niger* (epicalyxes) contained chlorogenic acid 1.1±0.1, quercetin-3*O*-glucoside-rhamnoside-rhamnoside (QGRR) and rutin 3.5±0.4 mg/g dry weight[81].

Chemical constituents of *Hyoscyamus reticulatus*:

Hyoscyamus reticulates was rich in tropane alkaloids, mainly hyoscyamine and scopolamine[51].

The main tropane alkaloid of the *H. reticulatus* plant was hyoscyamine in the range from 0.033 to 0.056% dry weight, followed by scopolamine from 0.011 to 0.015% dry weight[52].

The quantitative analysis of *Hyoscyamus reticulates* from Iran showed that it contained 0.031% hyoscyamine and 0.025% scopolamine[82].

The total alkaloid content of the leaves of *H. reticulatus* from Turkey was found to be in the range of 0.011-0.027%[83].

The maximum hyoscyamine and scopolamine concentrations were found in the leaf, and minimum concentration in the stem. Total alkaloids in the leaf, stem and capsule were 0.7126 , 0.2099 and 0.3686 mg/g respectively, and the total alkaloids in the leaf and root of cultured plant were 5.0844 and 0.8556 mg/g respectively. In leaf, stem and capsule of collected plants, hyoscyamine concentrations were 0.3515, 0.0788 and 0.3192 mg/g, and scopolamine concentrations were 0.3611, 0.1311 and 0.0494 mg/g respectively. However, in leaf and root of cultured plant, hyoscyamine concentrations were 2.3377 and 0.1683 mg/g, and scopolamine concentrations were 2.7467 and 0.6873 mg/g respectively[84].

From the *in vitro* hairy root cultures of *Hyoscyamus reticulates*, 10 tropane alkaloids were identified (hydrin, tropin, α-acetyltropin, 11-acetyltropin, cuscohygrin, apoatropin, littorin, hyoscyamine, scopolamine, 6-β-hydroxyhyos cyamine), and 4 from normal plant roots (apoatropin, littorin, hyoscyamine, scopolamine). However, the content of hyoscyamine and scopolamine in the leaves and roots of normal plants was maximal in and before flowering stage, and the maximal folar scopolamine content was before flowering. In the roots the changes in hyoscyamine and scopoamine production were not marked as in the leaves. The changes in the content of both main alkaloids in *Hyoscyamus reticulates* were greater in the leaves than in the roots during different growth periods[85].

The total phenolics in hexane and water extracts of *Hyoscyamus reticulatus* were found as 15.86 mgGAE/g and 24.25 mgGAE/g, respectively[86].

H. reticulatus (leaves) contained chlorogenic acid 3.4±0.1, quercetin-3*O*-glucoside-rhamnoside-rhamnoside (QGRR) 19.9±0.1 and rutin 8.9±0.3 mg/g dry weight. *Hyoscyamus niger* (epicalyxes) contained chlorogenic acid 1.8±0.1, quercetin-3*O*-glucoside-rhamnoside-rhamnoside (QGRR) 2.2±0.1 and rutin 0.1±0.0mg/g dry weight[81].

Analysis of the total lipid and fatty acid composition of the aerial parts of *Hyoscyamus reticulatus* revealed that the total saturated fatty acids was 12.45 % (myristic acid 0.23±0.01 %, pentadecylic acid 0.05±0.02 %, palmitic acid 8.69±1.81 %, margaric acid 0.15±0.38 % and stearic acid 3.33±1.00 %). The total monounsaturated fatty acids was 16.57 % (palmitoleic acid 0.18±0.05 % and oleic acid 16.39±1.43 %). The total polyunsaturated fatty acids was 70.97 % (linoleic acid 68.02±5.41 % and linolenic acid 2.95±1.36 %)[87].

Pharmacological effects:

Anti-diabetic effect:

The anti-diabetic potential of methanolic leaves extract of *Hyoscyamus albus* (was evaluated in diabetic rats. Streptozotocin-induced diabetic rats, were administered (100 and 200 mg/Kg bw) for 30 days. The oral administration of both doses of methanolic leaves extract of *Hyoscyamus albus* significantly reduced the levels of blood glucose and glycosylated hemoglobin in diabetic rats. Determination of plasma insulin levels revealed that the extract possessed insulin stimulating action[88].

Calystegines, polyhydroxylated alkaloids extracted from *Hyoscyamus albus* seeds were investigated for their *in vivo* antidiabetic effect on streptozotocine induced diabetes in mice. They markedly reduced blood glucose levels and lipid parameters of diabetic mice to normal concentrations after 20 days of treatment at

10mg/kg and 20mg/kg ($P<0.05$). Histopathological study of diabetic mice pancreas indicated that calystegines of *Hyoscyamus albus* have minimized streptozotocine damages on β-cells of islets of Langerhans, stimulated β-cells regeneration and improved insulin secretion[55].

Antioxidant effect:

In studying the antioxidant effects of Saudi medicinal plants (*Retama raetam*, *Salsola inermis*, *Hyoscyamus albus* and *Fagonia arabica*), the methanolic extracts of *Hyoscyamus albus* exhibited maximum DPPH antiradical, nitric oxide scavenging and metal chelating activities[57].

The antioxidant effect of *Hyoscyamus albus* leaves extracts was investigated using β-carotene bleaching method and DPPH assay. In the β-carotene bleaching test, the methanolic extract of *Hyoscyamus albus* leaves displayed highest antioxidant activity (76.00 %). The IC_{50} of antiradical activity of *Hyoscyamus albus* chloroform leaves extract was 330.19 ± 1.149 μg /ml[58].

The antioxidant activity of the crude extract of the leaves of *Hyoscyamus albus* was estimated using 2, 2-di- phenyl-1-picrylhydrazyl (DPPH) as free radical scavenger. Crude extract showed reducing potential correlated to the total phenolics and flavanoids contents[56].

The free radicals scavenging activity of seven fractions of alkaloidal extract of *Hyoscyamus niger* were evaluated by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay. Only one fraction of alkaloidal extract exhibited moderate free radical scavenging activity in comparison with the positive and negative controls[89].

The methanolic extracts of *Hyoscyamus niger* showed antioxidant activity (IC_{50}=1.64 μg) compared to α-tocopherol (IC_{50}=0.60 μg), which was used as the positive control[90].

The antioxidant activity of the aerial parts of *Hyoscyamus niger* extracts was invstigated with 2 methods DPPH (2, 2-diphenyl-1-picrylhydrazyl) and ferric reducing antioxidant power (FRAP) assays. The antioxidant (EC_{50}) for methanol extract was 377±1.21 μg/ml and it was 21±0.68 and 4.8±0.32 μg/ml for butylated hydroxytoluene (BHT) and ascorbic acid[45].

The antioxidant potential of aqueous extract of the aerial parts of *Hyoscyamus reticulatus* was studied using the ABTS scavenging capacity system. *Hyoscyamus reticulatus* aqueous extract exhibited significant antioxidant scavenging properties (533.26 μmol TE/g dry extract weight)[91].

The antioxidant capacities of hexane and water extracts of *Hyoscyamus reticulates* were screened by four different test systems including radical scavenging (DPPH assay), total antioxidant capacity, ferric and cupric reducing powers. The results revealed that water extract had higher antioxidant activity than hexane extract[86].

Antimicrobial effect:

The antimicrobial effects of *Hyoscyamus albus* leaves extracts was studied against three reference strains (*S. aureus* ATCC 25923, *E.coli* ATCC 25922, *P. aeruginosa* ATCC 27853), four clinical strains (*S.aureus, E coli P. aeruginosa, P. mirabilis*) and *Candida albicans.* The results showed that the butanolic extract of *Hyoscyamus albus* possessed antibacterial effects against *S. aureus* ATCC 25923, *S. aureus, E coli* ATCC 25922, *E coli, P. aeruginosa* ATCC 27853, *P. mirabilis* with MIC values of: 8.30, 6.00, 6.93, 8.32, 7.63, 7.53 mg/ml respectively. Methanolic extract also showed an antimicrobial activity against all the microbial strains except the *Candida albicans*[58]

The diameters of inhibition zone of water, hot water and methanol extracts of the leaves of *Hyoscyamus albus* against *Staphylococcus aureus* were 17, 17, 32 mm, against *Escherichia coli* 19, 17, 26 mm; against *Bacillus subtilis* 15, 20, 18 mm and against *Salmonella typhi* 10, 18, 24 mm respectively. The diameter of inhibition zone of the *Hyoscyamus albus* leaves alkaloids against *Staphylococcus aureus, Escherichia coli*; *Bacillus subtilis, Salmonella typhi,* methicillin-resistant and *Pseudomonas aeruginosa* were 41, 43, 34, 35,32 and 30 mm respectively[56].

Alkaloid extracts of *Hyoscyamus albus* showed antibacterial activity against *Pseudomonas stutzeri, Staphylococcus aureus, Escherichia coli* and *Klebsiella pneumonia*[92].

The methanol extracts of the seeds of *Hyoscyamus niger* were investigated for antimicrobial effect against urinary tract pathogens (*Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis* and *Candida albicans*). The extracts showed strong antimicrobial activity against *Enterococcus faecalis, Klebsiella pneumoniae* and *Candida albicans* with inhibition zones of 26.0, 19.0 and 16.0 mm, and moderate activity against the other test microorganisms[93].

The aqueous extract of *Hyoscyamus niger* seeds possessed dose dependent anticlostridial (*Clostridium petfringens*) activity (diameter of zone of growth inhibition 16-18mm)[94].

Hyoscyamus niger crude protein extract was tested against *E.coli, S. aureus, P. aeruginosa* and *P. vulgaris*. It showed diameters of growth inhibition zone of 14, 15, 14 and 20 mm against these pathogens respectively[95].

The methanolic extracts of the seeds of *Hyoscyamus niger* were investigated for anti fungal activity against six *Candida* species (*C. albicans* ATCC 10231, *C. tropicalis* ATCC 13808, *C. guilliermondii* ATCC 6260, *C. krusei* ATCC 20298, *C. glabrata* ATCC 2001 and *C. parapsilosis* ATCC 22019) and two *Cryptococcus species* (*C. neoformans* ATCC 90112 and *C. laurentii* ATCC 34142) The extract possessed strong antifungal potency. Greater activity was observed against both *Cryptococcus* species, with MIC values of 15 µg/ml[96].

The antifungal activity of a crude steroidal glycoside extract, fractions of spirostanoles and individual glicosides was investigated *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 kefyr* Y 0106, *Candida krusei* ATCC 6258 and *Candida lusitaniae* CBS 6936; Dermatophytes (one isolate of each species: *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Trichophyton soudanense*, *Microsporum canis*, *Microsporum gypseum*, *Epidermophyton fl occosum*, and *Cryptococcus neoformans*; filamentous fungi (one isolate of each species: *Aspergillus fumigatus, Aspergillus fl avus,Scopulariopsis brevicaulis*)]. *In vitro* spirostanol fraction and glycosides showed a broad spectrum of antifungal activity. Only slight differences in their fungicidal profi les were observed[72].

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. Hexane extract exhibited significant an antimicrobial effect as compared to water extract[86].

Insecticidal effect:

Methanol extract of *Hyoscyamus niger* aerial parts had positive effects on destroying the *Anopheles* spp larvae and the most effective extract for destroying the mosquitoes *Anopheles* spp larvae, was the flower extract (LC_{50} = 0/26 ppm)[97].

Antiasthmatic and antiallergic effects:

Hyoscyamus albus leaves extract also showed antiasthmatic and antiallergic activity. The results of the antiasthmatic activity revealed that the protective effect of extracts reached maximum effect after 4 hours of treatment against histamine (65% and 72% for methanol extracts at 100 and 200 mg/kg respectively). The results of the antiallergic activity showed that there was a significant reduction ($P \leq 0.05$) in leucocytes count in the groups treated by methanol extract 100mg/kg and 200 mg/kg (10.23±2.027% and 8.8±0.8287% respectively) in comparison with the groups treated with dexamethazone (8.475±1.127%) and control group (15.20±1.643%)[98].

Effect on gastrointestinal, respiratory and urinary smooth muscles:

The crude extract of *Hyoscyamus niger* seeds (Hn.Cr) exhibited antidiarrhoeal and antisecretory effects against castor oil induced diarrhoea and intestinal fluid accumulation in mice. The crude extract of *Hyoscyamus niger* seeds (Hn.Cr) caused a complete concentration-dependent relaxation of spontaneous contractions of rabbit jejunum, similar to that caused by verapamil, whereas atropine produced partial inhibition. Hn.Cr inhibited contractions induced by carbachol (1 microM) and K^+ (80 mM) in a pattern similar to that of dicyclomine, but different from verapamil and atropine. Hn.Cr shifted the Ca^{2+} concentration-response curves to the right, similar to that caused by verapamil and dicyclomine, suggesting a Ca^{2+} channel-blocking mechanism in addition to an anticholinergic effect. In the guinea-pig ileum, Hn.Cr produced a rightward parallel shift of the acetylcholine curves, followed by a non-parallel shift with suppression of the maximum response at a higher concentration, similar to that caused by dicyclomine, but different from that of verapamil and atropine. In guinea-pig trachea and rabbit urinary bladder tissues, Hn.Cr caused relaxation of carbachol (1 microM) and K^+ (80 mM) induced contractions at around 10 and 25 times lower concentrations than in gut, respectively, and shifted carbachol curves to the right. Only the organic fractions of the extract had a Ca^{2+} antagonist effect, whereas both organic and aqueous fractions had anticholinergic effect. A constituent, beta-sitosterol exhibited Ca^{2+} channel-blocking action. These results suggested that the antispasmodic effect of *Hyoscyamus niger* was mediated through a combination of anticholinergic and Ca^{2+} antagonist mechanisms. The relaxant effects of Hn.Cr occured at much lower concentrations in the trachea and bladder than intestinal[99]. *Hyoscyamus niger* (Hn.Cr) (0.3-3.0 mg/kg) also caused inhibition of the CCh (1 µmol/kg)-induced increase in the inspiratory pressure of anaesthetized rats[100].

Cardiovascular effects:

Hyoscyamus niger crude extract (Hn.Cr) caused a dose-dependent (10-100 mg/kg) fall in the arterial blood pressure (BP) of rats under anesthesia. In guinea-pig atria, Hn.Cr exhibited a cardiodepressant effect on

the rate and force of spontaneous atrial contractions. In isolated rabbit aorta, Hn.Cr (0.01-1.0 mg/ml) relaxed the phenylephrine (PE, 1 microM) and K^+ (80 mM)-induced contractions and suppressed PE (1 microM) control peaks obtained in Ca^{2+}-free medium similar to that caused by verapamil. The vasodilator effect of Hn.Cr was endothelium-independent as it was not opposed by N (omega)-nitro-L-arginine methyl ester in endothelium-intact rat aortic preparations and also occurred at a similar concentration in endothelium-denuded tissues[(101)].
The cardioprotective activity of the crude powder of the *Hyoscyamus niger* was studied in rats (100mg/100g bw). Many biochemical parameters like TGL, Ck-MB and LPO were evaluated to assess the cardioprotective effect of *Hyoscyamus niger* crude powder in isoproterenol induced myocardial injury. The oral administration of crude powder of *Hyoscyamus niger* water suspension against isoproterenol for 30 days, protected rats from the cardiac damage induced by lipid per oxidation and activation of antioxidant enzymes. It protected from cardiac necrosis as evidenced by the inhibitory activity on CK-Mb and TGL[(102)].

Antiinflammatory, analgesic and antipyretic effects:

The analgesic (acetic acid induced writhing response and the other formalin-induced paw licking in rats) and anti-pyretic properties (brewer's yeast induced fever in rats) of standardized *Hyoscyamus albus* methanolic extract were investigated experimentally. 100 and 200 mg/kg of *Hyoscyamus albus* methanolic extract decreased the acetic acid induced writhing responses and the licking time in the second phase of the formalin test. Moreover, it showed dose-dependent lowering of the body temperature up to 3h at both doses, the effect was comparable to that of paracetamol[(103-104)].

The methanolic extract of seeds of *Hyoscyamus niger* was evaluated for analgesic, anti-inflammatory and antipyretic activities in experimental animal models at different doses. The methanolic extract of seeds of *Hyoscyamus niger* produced significant increase in hot plate reaction time, while decreasing writhing response in a dose-dependent manner indicating analgesic activity. It was also effective in both acute and chronic inflammation evaluated by carrageenin-induced paw oedema and cotton pellet granuloma methods. It also exhibited antipyretic activity in yeast-induced pyrexia model[(77)].

The crude extract of *Hyoscyamus niger* (Hn.Cr) dose-dependently (50-100 mg/kg) reduced the numbers of acetic acid-mediated writhes in mice[(100)].

The analgesic effect of *Hyoscyamus niger* seeds alcoholic extract (500, 1000 and 2000 mg/kg bw, ip) was studied in acute and chronic pain in rats. The results revealed that injection of *Hyoscyamus niger* seeds alcoholic extract reduced the acute and chronic pain induced by formalin significantly ($P<0.001$) and significantly increased chronic pain threshold[(105)].

The antinociceptive effect of the metanolic extract of *Hyoscyamus reticulatus* was investigated in mice. Two models were used to study the effects of the extracts on nociception, acetic acid-induced writhing test and hot plate test in mice. The metanolic extract (50 mg/kg) possessed significant ($P<0.05$) analgesic activity comparable to diclophenac sodium, evidenced by increase in the reaction time by hot plate method and significant ($P<0.05$) reduction in acetic acid - induced writhings in mice with a maximum effect of 35.56 % reduction[(51)].

Hepatoprotective effect:

The hepatoprotective activity of methanolic extracts of leaves of *Hyoscyamus albus* was studied against hepatotoxicity induced by CCl_4. The extract protected the liver from the toxicity of CCl_4 and significantly ($P\leq0.05$) reduced the the biochemical markers TGO, TGP, ALP and BT elevated by CCl_4. Histological lesions induced by CCl_4 (necrosis, inflammatory cells infiltration and the congestion of the centrolobular vein) were absent in the group treated with *Hyoscyamus albus* extract[(98)].

Antihyperuricemic, and xanthine oxidase inhibitory effects:

The antihyperuricemic, and xanthine oxidase inhibitory potentials of *Hyoscyamus reticulates* were studied, the xanthine oxidase inhibitory activity of the extract was quantitated *in vitro* by measuring the decline in the catalytic rate of xanthine oxidase following incubations with the plant extracts and using xanthine as a substrate. The hypouricemic potential of the extract was evaluated using an *in vivo* model for hyperuricemia. *H. reticulatus* aqueous extract showed an inhibitory effect on xanthine oxidase activity (IC_{50}: 12.8 µg/ml). Oral administration of the aqueous extract significantly reduced serum urate levels in hyperuricemia induced in mice in a dose-dependent manner[(91)].

The aqueous extracts of eighteen Jordanian medicinal plants were evaluated for xanthine oxidase inhibitory potential at 200 µg/ml concentration. The aqueous extract of aerial parts of *Hyoscyamus reticulates* appeared as one of the most potent xanthine oxidase inhibitors (96.8% inhibition, IC_{50} =12.8 µg/ml)[(106)].

Anti- Parkinsonian:

The neuroprotective potential, of petroleum ether and aqueous methanol extracts of *Hyoscyamus niger* seeds was evaluated in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) model of Parkinson disease in mice. Parkinsonian mice were treated twice daily with the extracts (125–500 mg/kg, po) for two days and motor functions and striatal dopamine levels were assayed. Administration of the aqueous methanol extract (containing 0.03% w/w of L-DOPA), but not petroleum ether extract, significantly attenuated motor disabilities (akinesia, catalepsy and reduced swim score) and striatal dopamine loss in MPTP treated mice. The extract caused significant inhibition of monoamine oxidase activity and attenuated 1-methyl-4-phenyl pyridinium (MPP^+)-induced hydroxyl radical (OH) generation in isolated mitochondria, Accordingly, the protective effect of the methanolic extract of *Hyoscyamus niger* seeds against Parkinsonism in mice could be attributed to its inhibitory effects on the increased ·OH generated in the mitochondria[107].

The neuroprotective potential of methanol extract of *Hyoscyamus niger* (MHN) seeds was investigated in stereotaxically induced rotenone model of Parkinson's disease in rats. Rats were pretreated with MHN (125, 250, 500 mg/kg bw, po) once daily for 7 days and subjected to unilateral intrastriatal injection of rotenone (8 μg in 0.1 % ascorbic acid in normal saline). Three weeks after rotenone infusion, rats were tested for neurobehavioral activity and were sacrificed for estimation of lipid peroxidation (TBARS), total glutathione (GSH) content, and activity of antioxidant enzymes glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD) in brain homogenates. Administration of the MHN (containing L-DOPA) significantly attenuated motor disabilities (actophotometer, rotarod and Morris water maze test). Rat treated with rotenone showed reduced levels of thiobarbituric acid reactive substance (TBARS) and increased level of GSH content and antioxidants enzymes activities (GPX, SOD and CAT) in the MHN treated rats with Parkinson's disease. The extract showed presence of L-dopa with significant inhibition in DPPH, ABTS *in vitro* assay and monoamine oxidase activity[108].

Anticonvulsant effect:

The anticonvulsant effects of alcoholic extract of *Hyoscyamus niger* seed in doses of 50, 100 and 200 mg/kg ip, was evaluated in seizure induced by pentylene tetrazole. The results showed that administration of *Hyoscyamus niger* seed extract possessed inhibitory effect on the steps, progression and duration of seizure, especially in the last steps of convulsion. However, therapy with henbane seed extract resulted in an efficient anticonvulsive effect from the 8^{th} injection reaching the highest level of efficiency at the 12^{th} ($P<0.001$)[109].
The effects of methanolic extract of *Hyoscyamus niger* on seizures induced by picrotoxin was studied in mice. Groups of mice were pretreated with methanolic extract of the plant (12.5, 25, 50, 100, 200, 300, 400 mg/kg, ip), 20 minutes prior to the picrotoxin (12 mg/kg, ip)-induced seizures. The latency of seizure (sec), duration of seizure (sec) and mortality rate were determined in test and control groups. The results showed that latency of seizure was increased in groups pretreated with 100, 200, 300 and 400 mg/kg of extract, furthermore, methanolic extract also (200-400 mg/kg) significantly ($P<0.01$) delayed the death time in mice as compared to control[110].

Antidepressant effect:

The antidepressant effect of *Hyoscyamus niger* was evaluated in animal models [forced swim test (FST) and tail suspension test (TST) in mice] of depression with studying the possible mechanism underlying the antidepressant effect. Locomotor and anxiolytic activity was also studied. *Hyoscyamus niger* leaves ethanolic extract was administered to mice by oral route at dose of 25, 50, 100, 200 and 400 mg/kg for 14 days. An interaction of *Hyoscyamus niger* ethanolic extract with conventional antidepressant drugs were also studied at sub-effective doses. The ethanolic extract significantly reduced immobility duration of mice in FST and TST. The same doses did not change the motor activity in mice. However, high dose of extract showned anxiolytic activity. Interaction study with conventional antidepressant drugs reduced the duration of immobility count suggested, possible involvement of biogenic amine in antidepressant action[111].

Cytotoxic effect:

Alkaloidal extract of *Hyoscyamus niger* showed cytotoxic activity; it reduced the spontaneous frequency of chromosomal aberrations, micronuclei assay, and increased the mitotic index in mice bone marrow cells. The extract exhibited cytotoxic activity against cancer cell line Hep-2 in all periods of time, it had moderate cytotoxic effect on RD and AMN-3 and no effect on normal cell lines. Alkaloidal extract of *Hyoscyamus niger* also induced apoptosis activity rather than cytotoxic activity against cancer cell lines (A549, PC-3)[89].

Grossamide, and cannabisins D and G isolated from *Hyoscyamus niger* seeds exhibited moderate cytotoxicity in cultured LNCaP human prostate cancer cells[74].

Pharmacology of Tropane alkaloids:

Tropane alkaloids are anticholinergic drugs, hyoscyamine (atropine), and scopolamine (hyoscine) act primarily by competitive inhibition of the muscarinic actions of acetylcholine on structures innervated by postganglionic cholinergic neurons and in CNS, they produced wide range of pharmacological effects included: **Skin:** inhibition of sweating (hyperpyrexia may result), flushing; **Visual:** cycloplegia (relaxation of ciliary muscle), mydriasis (relaxation of sphincter pupillae muscle), increase in aqueous outflow resistance (increases intraocular pressure in many cases of glaucoma); **Digestive:** decreased salivation, reduced tone and motility in the gastrointestinal tract, decrease in vagus-stimulated gastric, pancreatic, intestinal, and biliary secretions; **Urinary:** urinary retention (relaxation of the detrusor muscle), relaxation of ureter; **Respiratory:** bronchial dilation and decreased secretions; **Cardiovascular:** bradycardia at low doses (may be a CNS effect) and tachycardia at higher doses (peripheral effect), increased cardiac output if patient is recumbent; **Central nervous system:** decreased concentration and memory, drowsiness; sedation, excitation; ataxia, asynergia, decrease in alpha EEG and increase in low-voltage slow waves (as in drowsy state); hallucinations; coma[112].

Hyoscyamine possesses many pharmacological effects, it has a high affinity for muscarinic receptors, acts both centrally and peripherally. Its general actions last about 4 hours except when placed topically in the eye, where the action may last for days. Its pharmacological effects included**: Eye**: it produced persistent mydriasis (dilation of the pupil), unresponsiveness to light, and cycloplegia (inability to focus for near vision). In patients with narrow-angle glaucoma, intraocular pressure may rise dangerously. **Gastrointestinal**: It reduced the motility of GI tract. **Urinary system**: It reduced hypermotility states of the urinary bladder. It is still occasionally used in enuresis among children. **Cardiovascular**: It produced divergent effects on the cardiovascular system, depending on the dose, at low doses, it decreased cardiac rate (bradycardia). With higher doses, the M2 receptors on the sinoatrial node were blocked, and the cardiac rate increased modestly. Arterial blood pressure was unaffected, but at toxic levels, it dilated the cutaneous vasculature. **Secretions**: it blocked the salivary glands, producing a drying effect on the oral mucous membranes (xerostomia). Secretion of sweat and lacrimal glands were also decreased. Therapeutically, atropine was used in many disorders included: **Ophthalmic**: exerted both mydriatic and cycloplegic effects, and it permited the measurement of refractive errors without interference by the accommodative capacity of the eye. **Antispasmodic**: It was used as an antispasmodic agent to relax the GI tract and bladder. **Antidote for cholinergic agonists**: It was used for the treatment of overdoses of cholinesterase inhibitor, insecticides and some types of mushroom poisoning (certain mushrooms contain cholinergic substances that block cholinesterases). Massive doses of the antagonist may be required over a long period of time to counteract the poisons. The ability of atropine to enter the central nervous system is of particular importance to minimize the CNS side effects of cholinergic drugs. **Antisecretory:** The drug was used as an antisecretory agent to block secretions in the upper and lower respiratory tracts prior to surgery[113].

Scopolamine (hyoscine), was used in medicine (in form of scopolamine hydrobromide,) for its depressant activity on the central nervous system, though it can cause delirium in the presence of pain, midrysis and cycloplegia. Combined with morphine, it produced amnesia and a tranquilized state known as twilight sleep. It was used in ophthalmogy to deliberately cause cycloplegia and mydriasis for diagnostic purposes and in the treatment of iridocyclitis. In otholaryngology, it was also used to dry the upper airway prior to the use of medical instrumentation on the airway. Scopolamine was also used as antiemetic, antivertigo, antispasmodic and was used in the pre-anestetic sedation, as an antiarrhithmic during anesthesia and for the prevention of motion sickness. Previously, it was also used in obstetrics, but now it considered dangerous[114].

Toxicity and side effects:

General side effects of tropane alkaloids:

Side effects of tropane alkaloids were depended on the dose, they included dry mouth, blurred vision, tachycardia, and constipation. Effects on the CNS include restlessness, confusion, hallucinations, and delirium, which may progress to depression, collapse of the circulatory and respiratory systems, and death. Low doses of cholinesterase inhibitors such as physostigmine may be used to overcome tropane alkaloids toxicity. In older individuals, the use of atropine to induce mydriasis and cycloplegia was considered to be too risky, because it may exacerbate an attack of glaucoma in someone with a latent condition. In other older individuals, atropine may induce urinary retention that was troublesome. Children were sensitive to effects of atropine—in particular, the rapid increases in body temperature that it may elicit. This may be dangerous in children[113].

***Hyoscyamus albus*:**

The acute toxicity study was performed on rats, the higher dose administration of 2000 mg/kg bw. of *Hyoscyamus albus* did not produce any toxic signs or deaths in rats. There were no significant differences ($P>0.05$) in the body and organ weights between control and treated groups. The (LD_{50}) of *Hyoscyamus albus*

was higher than 2000 g/kg bw. In subacute toxicity study, no mortality and toxic signs were observed with the doses of 100 and 200 mg/kg bw of extracts for 28 consecutive days[103-104].
Calystegines, polyhydroxylated alkaloids extracted from *Hyoscyamus albus* seeds were tested for their acute oral toxicity. Acute oral toxicity showed that calystegines were not toxic up to a dose of 2000mg/kg with absence of any signs of intoxication and damages in liver and kidney tissues[55].

***Hyoscyamus niger*:**

Hyoscyamus niger was a toxic plant because of its alkaloids contents and it may be fatal, all parts of *Hyoscyamus niger* were toxic and dryness or boiling could not destroy its alkaloids. There were several reports and case series of *Hyoscyamus niger* intoxication occurred accidentally or intentionally. Due to high concentration of scopolamine in *Hyoscyamus niger*, ingestion of high dose leads to hypertension, respiratory arrest, somnolence that followed by CNS excitation such as restlessness, hallucinations, delirium and manic episode. Symptoms and signs of the intoxicated patients (like atropine overdose), included mydriasis, tachycardia, arrhythmia, agitation, convulsion and coma. *Hyoscyamus niger* intoxication could induced dry mouth, thirst, slurred speech, difficulty in speaking, dysphagia, warm flushed skin, pyrexia, nausea, vomiting, headache, blurred vision and photophobia, urinary retention, distension of the bladder, drowsiness, hyper-reflexia, auditory, visual or tactile hallucinations, confusion, disorientation, delirium, aggressiveness, and combative behavior. Livestock poisoned by the plant showed constipation and colic (in horses), dryness of the mucosa in the upper digestive and respiratory tract, pupil dilation (mydriasis), alterations in the heart rate and CNS effects like ataxia, irritability, restlessness, seizures and respiratory depression[71,115-119]

***Hyoscyamus reticulates*:**

Oral ingestion of *Hyoscyamus reticulatus* may develop into many different types of clinical pictures ranging from an asymptomatic condition, through mild nausea, to life-threatening pathologies as depression of respiration[120].

During 1984-1989, 19 Bedouin children, 4-8 years old, were hospitalized because of *Hyoscyamus reticulatus* poisoning. The most prominent signs were altered state of consciousness (including deep coma in 3) and flushed dry, warm skin in all. Pupils were dilated in 18 of the 19, and restlessness and hallucinations were present in 17. Less common symptoms were vomiting, increased tendon reflexes, convulsions, involuntary movements, ataxia, hypertension, hyperpyrexia and tachycardia[121].

Six female patients aged from 19 to 49 poisoned after having ingested *Hyoscyamus reticulatus* showed that at least one of anticholinergic symptoms including flushing, mydriasis, dry mouth and tachycardia was present in all of the patients. In addition, different levels of agitation were observed in four of the patients. An euphoric emotional state was present in two patients. However, a prolongation of QT interval can accompany the anticholinergic symptoms of poisoning with *Hyoscyamus reticulates*[120].

II. CONCLUSION:

The current review discussed the chemical constituents, pharmacological and toxicological effects of *Hyoscyamus* species grown in Iraq.

REFERENCES:

[1]. Al-Snafi AE. Medicinal plants possessed antioxidant and free radical scavenging effects (part 3)- A review. IOSR Journal of Pharmacy 2017; 7(4): 48-62.
[2]. Al-Snafi AE. Anticancer effects of Arabian medicinal plants (part 1) - A review. IOSR Journal of Pharmacy 2017; 7(4): 63-102.
[3]. Al-Snafi AE. Medicinal plants for prevention and treatment of cardiovascular diseases - A review. IOSR Journal of Pharmacy 2017; 7(4): 103-163.
[4]. Al-Snafi AE. Antimicrobial effects of medicinal plants (part 3): plant based review. IOSR Journal of Pharmacy 2016; 6(10): 67-92.
[5]. Al-Snafi AE. A review of medicinal plants with broncho-dilatory effect- Part 1. Scholars Academic Journal of Pharmacy 2015; 5(7): 297-304.
[6]. Al-Snafi AE. Medicinal plants affected reproductive systems (part 2) - plant based review. Sch Acad J Pharm 2016; 5(5): 159-174.
[7]. Al-Snafi AE. The pharmacological and therapeutic importance of *Eucalyptus* species grown in Iraq. IOSR Journal of Pharmacy 2017; 7(3): 72-91.
[8]. Al-Snafi AE. A review on *Dodonaea viscosa*: A potential medicinal plant. IOSR Journal of Pharmacy 2017; 7(2): 10-21.
[9]. Al-Snafi AE. Pharmacological and therapeutic importance of *Desmostachya bipinnata*- A review. Indo Am J P Sci 2017; 4(01): 60-66.

[10]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Eryngium creticum*- A review. Indo Am J P Sci 2017; 4(01): 67-73.
[11]. Al-Snafi AE. The pharmacology of *Equisetum arvense*- A review. IOSR Journal of Pharmacy 2017; 7(2): 31-42.
[12]. Al-Snafi AE. A review on *Erodium cicutarium*: A potential medicinal plant. Indo Am J P Sci 2017; 4(01): 110-116.
[13]. Al-Snafi AE. Pharmacology of *Echinochloa crus-galli* - A review. Indo Am J P Sci 2017; 4(01): 117-122.
[14]. Al-Snafi AE. The pharmacological potential of *Dactyloctenium aegyptium*- A review. Indo Am J P Sci 2017; 4(01): 153-159.
[15]. Al-Snafi AE. Chemical constituents, pharmacological and therapeutic effects of *Eupatorium cannabinum*- A review. Indo Am J P Sci 2017; 4(01): 160-168.
[16]. Al-Snafi AE. Nutritional and therapeutic importance of *Daucus carota*- A review. IOSR Journal of Pharmacy 2017; 7(2): 72-88.
[17]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Dalbergia sissoo* - A review. IOSR Journal of Pharmacy 2017; 7(2): 59-71.
[18]. Al-Snafi AE. Medical importance of *Datura fastuosa* (syn: *Datura metel*) and *Datura stramonium* - A review. IOSR Journal of Pharmacy 2017; 7(2):43-58.
[19]. Al-Snafi AE. Phytochemical constituents and medicinal properties of *Digitalis lanata* and *Digitalis purpurea* - A review. Indo Am J P Sci 2017; 4(02): 225-234.
[20]. Al-Snafi AE. Therapeutic and biological activities of *Daphne mucronata* - A review. Indo Am J P Sci 2017; 4(02): 235-240.
[21]. Al-Snafi AE. Pharmacological and therapeutic importance of *Erigeron canadensis* (Syn: *Conyza canadensis*). Indo Am J P Sci 2017; 4(02): 248-256.
[22]. Al-Snafi AE. *Eschscholzia californica*: A phytochemical and pharmacological review. Indo Am J P Sci 2017; 4(02): 257-263.
[23]. Al-Snafi AE. Pharmacology and therapeutic potential of *Euphorbia hirta* (Syn: *Euphorbia pilulifera*) - A review. IOSR Journal of Pharmacy 2017; 7(3): 7-20.
[24]. Al-Snafi AE. A review on *Fagopyrum esculentum*: A potential medicinal plant. IOSR Journal of Pharmacy 2017; 7(3): 21-32.
[25]. Al-Snafi AE. Nutritional and pharmacological importance of *Ficus carica* - A review. IOSR Journal of Pharmacy 2017; 7(3): 33-48.
[26]. Al-Snafi AE. Pharmacological and therapeutic importance of *Echium italicum*- A review. Indo Am J P Sci 2017; 4(02): 394-398.
[27]. Al-Snafi AE. Therapeutic importance of *Ephedra alata* and *Ephedra foliata*- A review. Indo Am J P Sci 2017; 4(02): 399-406.
[28]. Al-Snafi AE. Therapeutic potential of *Erodium cicutarium* - A review. Indo Am J P Sci 2017; 4(02): 407-413.
[29]. Al-Snafi AE. Pharmacology of *Ficus religiosa*- A review. IOSR Journal of Pharmacy 2017; 7(3): 49-60.
[30]. Al-Snafi AE. Chemical contents and medical importance of *Dianthus caryophyllus*- A review. IOSR Journal of Pharmacy 2017; 7(3): 61-71.
[31]. The plant list, *Hyoscyamus niger*, http://www.theplantlist.org/tpl/ record/kew-2857441
[32]. The plant list, *Hyoscyamus albus*, http://www.theplantlist.org/tpl/ record/kew 2857395
[33]. The plant list, *Hyoscyamus reticulates*, http:// www. Theplantlist .org/tpl/ record/ kew- 2857459
[34]. ITIS, *Hyoscyamus albus*, https://www.itis.gov/servlet/SingleRpt/SingleRpt? Search_ topic=TSN&search_value=503125#null
[35]. ITIS, *Hyoscyamus niger*, https://www.itis.gov/servlet/SingleRpt/SingleRpt? Search_ topic=TSN&search_value=30523#null
[36]. U.S. National Plant Germplasm System, *Hyoscyamus albus*, https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?316078
[37]. U.S. National Plant Germplasm System, *Hyoscyamus niger*, https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?19532
[38]. U.S. National Plant Germplasm System, *Hyoscyamus reticulates*, https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?408142
[39]. Flora of China, Hyoscyamus, http://www.efloras.org/florataxon.aspx?flora_id= 2&taxon_id=116158
[40]. Flora of Pakistan, Hyoscyamus, http://www.efloras.org/florataxon. aspx? flora_id=5 &taxon _ id= 116158

[41]. El Bazaouia A, Bellimamb A, Lançarc IT and Soulaymania A. Gas-liquid chromatography -mass spectrometry investigation of tropane alkaloids in *Hyoscyamus albus* L. from Morocco. Z Naturforsch 2012; 67 c, 461 – 465.
[42]. Bellakhdar J. La pharmacopée marocaine traditionnelle (médecine arabe ancienne et savoirs populaires). Ibis Press, Saint-Etienne 1997:494-496.
[43]. Matsuda J, Okabe S, Hashimoto T and Yamaday. Cultured roots of *Hyoscyamus niger*. J Biology Chemistry 1991; 25(15):460-464.
[44]. Nadkarni KM. Indian materia medica. Mumbai: Bombay popular prakashan 2002; 1: 670-72.
[45]. Hajipoor K, Sani AM and Mohammad A. *In vitro* antioxidant activity and phenolic profile of *Hyoscyamus niger*. IJBPAS 2015; 4(7): 4882-4890.
[46]. Zargari A. Medicinal Plants. 5th ed. Tehran University Publications, Tehran, 1990: 570-575.
[47]. Bown D. Encyclopedia of Herbs and their Uses. 1st ed., Dorling Kindersley, London, New York, Stuttgart, Moscow, 1995: 317.
[48]. Chevallier A. The Encyclopedia of Medicinal Plants. Dorling Kindersley Publishers, London, UK 1996.
[49]. Duke JA.. CRC Handbook of Medicinal Herbs. CRC Press, Boca Raton, 1985: 297-300.
[50]. Aparna. K, Joshi Abhishek J and Vyas M. Phytochemical and pharmacological profile of *Hyoscyamus niger* Linn (Parasika Yavani)- A review. Pharma Science Monitor 2015; 6(1): 153-158.
[51]. Oto G, Ozdemir H, Yaren B, Yetkin Y, Tas A, Tanrıtanır P and Öztürk F. Antinociceptive activity of methanol extract of *Hyoscyamus reticulatus L.* in mice. American Journal of Phytomedicine and Clinical Therapeutics 2013; 1(2):117-123.
[52]. Medicinal Plants, *Hyoscyamus reticulatus* L,. http:// medicinalplants. us/ hyoscyamus -reticulatus-l
[53]. Henbane, side effects and health benefits, https://www.herbal-supplement-resource. com/henbane.html
[54]. Yasin JN. Flora of Pakistan. Pakistan Agricultural Research Council, Islamabad, Pakistan, 1985: 168.
[55]. Bourebaba L, Saci S, Touguit D, Gali L, Terkmane S, Oukil N and Bedjou F. Evaluation of antidiabetic effect of total calystegines extracted from *Hyoscyamus albus*. Biomed Pharmacother 2016; 82: 337-344.
[56]. Alghazeer R, El-Saltani H, Saleh N, Al-Najjar A and Hebail F. Antioxidant and antimicrobial properties of five medicinal Libyan plants extracts. Natural Science 2012; 4: 324-335.
[57]. Mobin M, Khan MN and Abbas ZK. Ecotype difference in bioactive constituents and *In vitro* antioxidant activities of some Saudi medicinal plants. European Journal of Medicinal Plants 2015; 7(3): 125-136.
[58]. Benhouda A, Yahia M, Benhouda D, Bousnane NE, Benbia S, Hannachi NE and Ghecham A. Antimicrobial and antioxidant activities of various extracts of *Hyoscyamus albus* L. and *Umbilicus rupestris* L. leaves. Algerian Journal of Natural Products 2014; 2(1): 4-17.
[59]. Parr AJ, Payne J, Eagles J, Champan BT, Robins RJ and Rhodes MJC. Variation in tropane alkaloids accumulation within the Solanaceae and strategies for its exploitation. Phytochemistry 1990; 29: 2545-2550.
[60]. Doerk-Schmitz K, Witte L and Alfermann AW. Tropane alkaloid patterns in plants and hairy roots of *Hyoscyamus albus.* Phytochemistry 1994; 35: 107-110.
[61]. El-Shazly A, Tei A, Witte L, El-Domiaty M and Wink M. Tropane alkaloids of *Hyoscyamus boveanus*, *H. desertorum*, *H. muticus* and *H. albus* from Egypt. Z Naturforsch 1997; 52c:729-739.
[62]. Doerk K, Witteb L and Alfermann AW. Identification of tropane alkaloids in hairy root cultures of *Hyoscyamus albus.* Z Naturforsch 1991; 46c, 519-521.
[63]. Mahmood U, Shukla YN and Thakur RS. 2,3-dimethylnonacosane and tropane alkaloids from *Hyoscyamus albus*. Phytochemistry 1985; 24(7):1618-1619·
[64]. Hibi N, Fujita T, Hatano M, Hashimoto T and Yamada Y. Putrescine N-methyl-transferase in cultured roots of *Hyoscyamus albus*: n-butylamine as a potent inhibitor of the transferase both *in vitro* and *in vivo*. Plant Physiol 1992; 100(2): 826-835.
[65]. Hashimoto T, Yukimune Y and Yamada Y. Putrescine and putrescine N-methyl-transferase in the biosynthesis of tropane alkaloids in cultured roots of *Hyoscyamus albus*: I. Biochemical studies. Planta 1989;178(1):123-130.
[66]. Hashimoto T, Yukimune Y and Yamada Y. Putrescine and putrescine N-methyl-transferase in the biosynthesis of tropane alkaloids in cultured roots of *Hyoscyamus albus*: II. Incorporation of labeled precursors. Planta. 1989; 178(1): 131-137.
[67]. Kawauchi M, Arima T, Shirota O, Sekita S, Nakane T, Takase Y and Kuroyanagi M. Production of sesquiterpene-type phytoalexins by hairy roots of *Hyoscyamus albus* co-treated with cupper sulfate and methyl jasmonate. Chem Pharm Bull (Tokyo) 2010; 58(7): 934-938.
[68]. Sharova ESh, Aripova SU and Abdylalimov OA. Alkaloids from *Hyoscyamus niger* and *Datura stramonium*. Chemistry of Natural Compounds 1977; 13(1): 117-118.

[69]. Pudersell K, Vardja T, Vardja R, Matto V, Arak E and Raal A. Inorganic ions in the medium modify tropane alkaloids and riboflavin output in *Hyoscyamus niger* root cultures. Pharmacognosy Magazine 2012; 8(29): 73-77.
[70]. Zhang W, Zhang W, Luo J and Kong L. A new steroidal glycoside from the seeds of *Hyoscyamus niger***.** Journal Natural Product Research, Formerly Natural Product Letters 2013; 27(21): 1971-1974.
[71]. Alizadeh A, Moshiri M, Alizadeh J and Balali-Mood M. Black henbane and its toxicity – a descriptive review. AJP 2014; 4(5): 297-311.
[72]. Lunga I, Chintea P, Shvets S, Favel A and Pizza C. Steroidal glycosides from the seeds of *Hyoscyamus niger* and their antifungal activity. Chemistry Journal of Moldova 2007; 2 (1): 108-113.
[73]. Lunga I, Kintia P, Shvets S, Bassarello C, Pizza C and Piacente S. Three spirostanol glycosides from the seeds of *Hyoscyamus niger* L. Chemistry Journal of Moldova 2006; 1: 123-127.
[74]. Ma CY, Liu WK and Che CT. Lignanamides and nonalkaloidal components of *Hyoscyamus niger* seeds. J Nat Prod 2002; 65 (2): 206-209.
[75]. Begum AS, Verma S, Sahai M, Schneider K and Süssmuth R. Hyoscyamal, a new tetrahydrofurano lignan from *Hyoscyamus niger* Linn. Nat Prod Res 2009; 23(7): 595-600.
[76]. Sajeli B, Sahai M, Suessmuth R, Asai T, Hara N and Fujimoto Y. Hyosgerin, a new optically active coumarinolignan, from the seeds of *Hyoscyamus niger*. Chem Pharm Bull (Tokyo) 2006; 54(4): 538-541.
[77]. Begum S, Saxena B, Goyal M, Ranjan R, Joshi VB, Rao ChV, Krishnamurthy S and Sahai M. Study of anti-inflammatory and antipyretic activities of seeds of *Hyoscyamus niger* and isolation of a new coumarinolignan. Fitoterapia 2010; 81: 178-184.
[78]. Ma CY, Williams ID and Che CT. Withanolides from *Hyoscyamus niger* seeds. J Nat Prod 1999; 62 (10): 1445–1447.
[79]. Steinegger E and Sonanini D. Solanaceous flavones. II. Flavones of *Hyoscyamus niger*. Pharmazie 1960; 15: 643-644.
[80]. Begum AS. Bioactive Non-alkaloidal secondary metabolites of *Hyoscyamus niger* Linn seeds: A review. Research Journal of Seed Science 2010; 3: 210-217.
[81]. Jassbi AR, Miri R, Masroorbabanari M, Asadollahi M, Attarroshan M and Baldwin IT. HPLC-DAD-ESIMS analyses of *Hyoscyamus niger* and *H. reticulatus* for their antioxidant constituents. Austin Chromatogr 2014;1(5): 1022.
[82]. Ghassemi N, Sajjadi SE and Saghai F. A study on morphology and phytochemistry of *Hyoscyamus reticulates* L. DARU Journal of Pharmaceutical Sciences 1995; 5(1-2): 1-10.
[83]. Kartal M, Kurucu S, Altun L, Ceyhan T, Sayar E, Cevheroglu S and Yetkin Y. Quantitative analysis of l-hyoscyamine in *Hyoscyamus reticulatus* L by GC-MS. Turk J Chem 2003; 27: 565-569.
[84]. Moradi B, Delfan B, Hashemi P, Mousavi A and Rahnama H. Matrix solid phase dispersion extraction for tropane alkaloid detection in cultured and collected *Hyoscyamus reticulatus* plants. International Journal of Advanced Research 2015; 3(11): 78 – 82.
[85]. Ionkova I. Alkaloid production of *Hyoscyamus reticulates* plant and transformed root culture clone. Biotechnology & Biotechnological Equipment 1992; 6(2): 50-52.
[86]. Güneş E, Zengin G, Uysal A, Aktümsek A and Durak Y. A study on antioxidant and antimicrobial properties of hexane and water extracts from *Hyoscyamus reticulatus*. SUFEFD 2014; 39: 21-29.
[87]. Keskin1 C, Yavuz C and Kaçar S. Determination of fatty acid compositions of total lipid, phospholipid and triacylglycerol fractions of aboveground parts of four species of the genus *Hyoscyamus.* Chemistry Research Journal 2016; 1(5):1-8.
[88]. BenhoudaA, Yahia M, Khadhraoui H, Benbia S and Benhouda D. Hypoglycemic activity of methanolic extract of *Hyoscyamus albus* l. leaves in straptozotocin induced diabetic rats. Nat Prod Chem Res 2014; 2:5.
[89]. Ismeel AO. Cytogenetic and cytotoxic studies on the effect of phytoinvestigated active compounds of *Hyoscyamus nige*r (*in vivo* and *ex vivo*). PhD thesis, Al-Nahrain University- College of Science, Iraq 2011.
[90]. Souri E, Amin G, Dehmobed-Sharifabadi A, Nazifi A and Farsam H. Antioxidative activity of sixty plants from Iran. Iranian Journal of Pharmaceutical Research 2004; 3: 55-59.
[91]. Mohammad MK, Almasri IM, Tawaha K, Issa A, Al-Nadaf A, Hudaib M, Alkhatib HS, Abu-Gharbieh E and Bustanji Y. Antioxidant, antihyperuricemic and xanthine oxidase inhibitory activities of *Hyoscyamus reticulatus*. Pharm Biol 2010; 48(12): 1376-1383.
[92]. Kadi K, Yahia A, Hamli S, Auidane L, Khabthane H and Ali WK. *In vitro* antibacterial activity and phytochemical analysis of white henbane treated by phytohormones. Pak J Biol Sci 2013; 16(19): 984-990.

[93]. Dulger G and Dulger B. Antimicrobial activity of the seeds of *Hyoscyamus niger* L (Henbane) on microorganisms isolated from urinary tract infections. Journal of Medicinal Plants Studies 2015; 3(5): 92-95
[94]. Akhtar MS and GiII SA. Evaluation of anticlostridial efficacy of indigenous medicinal plant drugs: Rasoot, Ajwain Khurasani Neem and Bakain. Pak J Agli Sci 1992; 29(4): 371-375.
[95]. Mateen A, TanveerZ, Janardhan K and Gupta VC. Screening and purification of antibacterial proteins and peptides from some of the medicinal plants seeds. Int J Pharm Bio Sci 2015; 6(4): 774-781.
[96]. Dulger B, Hagioglu N, Goncu BS and Gucin F. Antifungal activity of seeds of *Hyoscyamus niger* L. (Henbane) against some clinically relevant fungal pathogens. Asian Journal of Chemistry 2010; 22(8): 6321-6324.
[97]. Behravan M, Vaezi Kakhki MR and Baharshahi A. Comparing larvicidal effect of methanol extract of the aerial parts of henbane (*Hyoscyamus niger* L) and oleander (Neriumoleander L) plants on *Anopheles* spp larvae (Diptera: culicidae) *in vitro*. Zahedan Journal of Researches in Medical Sciences. 2017; 19(3): e8631.
[98]. Benhouda A, Mouloud Y, Hachani K, Nassiba C, Hadjar B, Souhila B and Djahida B. *In vivo* evaluation of hepatoprotective, antiasthmatic and antiallergic activities of methanolic extracts of leaves of *Hyoscyamus albus* L (Solanaceae) and *Umbilicus rupestris* L (Crassulaceae). The 15th International Congress of the International Society for Ethno-Pharmacology, Shoubak University College, 2015:3.
[99]. Gilani AH, Khan AU, Raoof M, Ghayur MN, Siddiqui BS, Vohra W and Begum S. Gastrointestinal, selective airways and urinary bladder relaxant effects of *Hyoscyamus niger* are mediated through dual blockade of muscarinic receptors and Ca^{2+} channels. Fundam Clin Pharmacol 2008; 22(1): 87-99.
[100]. Khan A and Gilani AH. *In vivo* Studies on the bronchodilatory and analgesic activities of *Hyoscyamus niger* and *Aspalathus linearis*. Lat Am J Pharm 2010; 29 (5): 777-782.
[101]. Khan AU and Gilani AH. Cardiovascular inhibitory effects of *Hyoscyamus niger*. Methods Find Exp Clin Pharmacol 2008; 30(4): 295-300.
[102]. Vallabi DE and Elango V. Preliminary studies on cardio protective effect of *Hyoscyamus niger* Linn in male albino rats. Journal of Chemical and Pharmaceutical Research 2016; 8(7): 860-864
[103]. Benhouda A and Yahia M. Toxicity, analgesic and anti-pyretic activities of methanolic extract from *Hyoscyamus albus* leaves in albinos rats. Planta Med 1999; 65(1):60-63.
[104]. Massinissa Y, Affaf, H and Mouloud Y. Analgesic, toxicity and anti-pyretic activities of methanolic extract from *Hyoscyamus albus* leaves in albinos rats. International Journal of Biotechnology and Bioengineering 2014; 1(8):72.
[105]. Ghosian MH , Moradi M and Yaghout poor E. Assessment of *Hyoscyamus niger* seeds alcoholic extract effects on acute and chronic pain in male NMRI rats. Basic and Clinical Pathophysiology 2012; 1(1): 29-36.
[106]. Bustanji Y, Hudaib M, Tawaha K, Mohammad MK, Almasri I, Hamed S and Oran S. *In vitro* xanthine oxidase inhibition by selected Jordanian medicinal plants. Jordan Journal of Pharmaceutical Sciences 2011; 4(1): 49 -56.
[107]. Sengupta, T., Vinayagam, J., Nagashayana, N. *et al*. Antiparkinsonian effects of aqueous methanolic extract of *Hyoscyamus niger* seeds result from its monoamine oxidase inhibitory and hydroxyl radical scavenging potency. Neurochem Res 2011; 36: 177-186.
[108]. Khatri DK and Juvekar AR. Propensity of *Hyoscyamus niger* seeds methanolic extract to allay stereotaxically rotenone-induced Parkinson's disease symptoms in rats. Orient Pharm Exp Med 2015; 15:387–388.
[109]. Kiasalari Z, Khalili M and Heidari H. Anti-convulsant effect of alcoholic *Hyoscyamus niger* L seed extract on PTZ model of kindling in male mice. Razi Journal of Medical Sciences 2011; 18(85): 27-33.
[110]. Reza HM, Mohammad H, Golnaz E and Gholamreza S. Effect of methanolic extract of *Hyoscymus niger* L on the seizure induced by picritoxin in mice. Pak J Pharm Sci 2009; 22(3): 308-312
[111]. Patil AD, Patil AY and Raje AA. Antidepressant like property of *Hyoscyamus niger* Linn. in mouse model of depression. Innovations in Pharmaceuticals and Pharmacotherapy 2013; 1 (2): 60-69.
[112]. Craig CR and Stitzel RE. Modern Pharmacology with clinical applications. 6th ed. Lippincott Williams & Wilkins, 2004.
[113]. Pharmacological Blog, Atropine, http://n-pharmacology.blogspot.com/ 2013/ 06/ atropine.html
[114]. De Simone R, Margarucci, L and De Feo V. Tropane alkaloids: An overview. Pharmacologyonline 2008; 1: 70-89.
[115]. Graev M and Fallani M. Collective poisoning caused by ingestion of *Hyoscyamus niger* (with a fatal case). Minerva Medicoleg 1960; 80: 225-230.
[116]. Grieve M. A Modern Herbal, 1913, http://botanical.com/botanical/ mgmh/h/ henban23.html.

[117]. Anonymous. *Hyoscyamus niger*, black henbane. The poison garden. Website 2013, http://www. thepoisongarden. co.uk/atoz/hyoscyamus_niger.htm.
[118]. Barron P and Jordan L. *Hyoscyamus niger:* A case series analysis. The Australian Journal of Homoeopathic Medicine 2009; 21(1): 34-38.
[119]. Collak Z, Kara D, Karaman EU, Karakoc F and Collak A. *Hyoscyamus niger* intoxication: A case report. British Journal of Medicine & Medical Research 2016; 11(6): 1-3.
[120]. Aslan S, Cakir Z, Emet M, Aksakal E, Akoz A and Uzkeser M. Wildflower (*Hyoscyamus reticulatus*) causes QT prolongation. Bratisl Lek Listy 2013; 114(6): 333-336.
[121]. Urkin J, Shalev H, Sofer S and Witztum A. Henbane (*Hyoscyamus reticulatus*) poisoning in children in the Negev. Harefuah 1991;120(12):714-716.

Prof Dr Ali Esmail Al-Snafi " Therapeutic importance of Hyoscyamus species grown in Iraq (Hyoscyamus albus, Hyoscyamus niger and Hyoscyamus reticulates)- A review ” IOSR Journal of Pharmacy (IOSRPHR), vol. 8, no. 06, 2018, pp. 18-32