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The chemical constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia*- A review

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Abstract: The phytochemical studies showed that *Convolvulus arvensis* contained alkaloids, phenolic compounds, flavonoids, carbohydrates, sugars, mucilage, sterols, resin. tannins, unsaturated sterols/triterpenes, lactones and proteins; while, *scammonia* contained scammonin resin, dihydroxy cinnamic acid, beta-methyl-esculetin, ipuranol, surcose, reducing sugar and starch. The previous pharmacological studies revealed that *Convolvulus arvensis* possessed cytotoxic, antioxidant, vasorelaxat, immunostimulant, epatoprotective, antibacterial, antidiarrhoeal and diuretic effect; while, *Convolvulus scammonia* sowed purgative , vasorelaxat, anti platelet aggregation, anticancer and cellular protective effects. This study will highlight the constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia.*

Keywords: *constituents, pharmacology, Convolvulus arvensis, Convolvulus scammonia.*

I. INTRODUCTION:

Herbal medicine is the oldest form of medicine known to mankind. It was the mainstay of many early civilizations and still the most widely practiced form of medicine in the world today. Plant showed wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects[1-40]. Plants generally produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of many pharmaceutical drugs. *Convolvulus arvensis* and *Convolvulus scammonia* of the genus *Convolvulus* were grown in Iraq. The phytochemical studies showed that *Convolvulus arvensis* contained alkaloids, phenolic compounds, flavonoids, carbohydrates, sugars, mucilage, sterols, resin. tannins, unsaturated sterols/triterpenes, lactones and proteins; while, *scammonia* contained scammonin resin, dihydroxy cinnamic acid, beta-methyl-esculetin, ipuranol, surcose, reducing sugar and starch. The previous pharmacological studies revealed that *Convolvulus arvensis* possessed cytotoxic, antioxidant, vasorelaxat, immunostimulant, epatoprotective, antibacterial, antidiarrhoeal and diuretic effect; while, *Convolvulus scammonia* sowed purgative, vasorelaxat, anti platelet aggregation, anticancer and cellular protective effects. This study will highlight the constituents and pharmacological effects of *Convolvulus arvensis* and *Convolvulus scammonia.*

II.PLANTS PROFILE:

1- *Convolvulus arvensis*

Synonyms:

Convolvulus ambigens House, *Convolvulus incanus* Vahl, *Strophocaulos arvensis* (L.) Small[41].

Taxonomic classification:

Kingdom: Plantae; **Phylum**: Magnoliophyta; **Class**: Magnoliopsida; **Order**: Solanales; **Family**: Convolvulaceae; **Genus**: *Convolvulus*; **Species**: *Convolvulus arvensis*[41-43].

Nomenclature and common names:

Convolvulus is derived from the Latin (*convolere*) meaning to entwine, and *arvensis* means (of fields)[42]. Common names of the plant were**: Afrikaans**: akkerwinde, klimop; **Arabic**: leblab elhokul**,** ullayq, ullayq bari, laf, laf elkamh; **Brazil**: campainha, corda-de-viola; **Chinese**: tian xuan hua**; English**: bindweed, common bindweed, field bindweed, lesser bindweed, small bindweed, white convolvulus, wild morning-glory; **French**: liseron des champs; **German**: Akerwinde; Spanish: corregüela; and **Swedish**: åkervinda[43].

Distribution:

It was distributed in **Africa**: Algeria, Egypt, Libya, Morocco and Tunisia; **Asia**: Afghanistan, Cyprus, Iran, Palstine, Jordan, Lebanon, Syria, Turkey, Armenia, Azerbaijan, Georgia, Russian Federation, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, Mongolia, China, India, Nepall and Pakistan; **Europe**:

Denmark, Finland, Ireland, Norway, Sweden, United Kingdom, Austria, Belgium, Czechoslovakia, Germany, Hungary, Netherlands, Poland, Switzerland, Belarus, Estonia, Latvia, Lithuania, Moldova, Russian Federation, Albania, Bulgaria, Former Yugoslavia, Greece, Italy, Romania, France, Portugal and Spain[43].

Description:

Field bindweed is a perennial vine (0.4-2 inches in height) arising from deep, persistent, spreading roots. Leaves: are dull green with readily visible veins. The petiole is flattened, and grooved on the upper side. The first true leaves are dull green and may be covered with fine granules on the upper surface. Leaves of this species are extremely variable, possibly reflecting variability in soil moisture and fertility. The most common leaf type is hastate or sagittate, which means they have distinctive arrowhead shapes with pointed lobes at the bases. Some leaves are round, ovate or oblong, and some may even be linear. These deviations from the typical leaf types may be found on plants growing in disturbed conditions**.** Stems: are slender vines that run along the ground or climb any available object. Stem length ranges from one to six feet (0.3-1.8 m), they often twine, form dense, tangled mats, and they are normally hairless but can be pubescent. Flowers: have five fused petals forming a 2-2.5 cm long funnel-like corolla. Petals are generally white to very pale pink. The sepals are approximately 5mm long, oblong and separate. Five stamens of unequal lengths are attached to the base of the corolla. The pistil is compound with two thread-like stigmas. Fruits: each fruit is about 8mm wide, rounded, light brown. Seeds are dark brown to black, and have rough surfaces. They are 0.5-1.2 cm long, and their shapes vary, depending on the number produced in the fruit; they are rounder when only one is produced and progressively thinner as more are produced. Field bindweed fruits usually contain 2 seeds, but 1-4 seeds are not uncommon; an anomalous Russian specimen was found with 10 seeds in a capsule. Roots: field bindweed produces an extensive system of roots and rhizomes whitish in colour, cordlike, and fleshy. The primary root forms a taproot that can penetrate the soil to depths of two to ten feet (0.5-3 m). Lateral roots grow from buds along the taproot and from adventitious buds at the stem base[44-45].

Traditional uses:

The plant was reported to have used in traditional medicine system from as early as 1730s. Aerial parts of *convolvulus arvensis* was used as laxative, wound healing, anti-spasmodic anti-haemorrhagic, anti-angiogenetic and for the treatment of parasites and jaundice[46-50]. In addition it was used as diuretic and in skin disorders such as anti-furunculosis, antidandruff and in spider bites[51]. *Convolvulus arvensis* was also used traditionally as decoction in cough and flu, to treat the painful joints, inflammation and swelling[52].

Physicochemical characteristics of aerial parts of *Convolvulus arvensis*:

Total Ash 6.1 %w/w , acid insoluble ash 4.52 %w/w, water soluble ash 5.85% w/w, alcohol extractive substances 12.19% w/w, ether soluble substances 5% w/w and CHCl3 soluble substances 8% w/w[53].

Chemical constituents:

Phytochemical studies showed that *Convolvulus arvensis* L. contained alkaloids, phenolic compounds, flavonoids, carbohydrates, sugars, mucilage, sterols, resin. tannins, unsaturated sterols/triterpenes, lactones and proteins[53-59].

Convolvulus arvensis was found to contain the tropane alkaloids, tropine, pseudotropine, tropinone as well as cuscohygrine, meso-cuscohygrine and calystegines[60-61].

Aerial parts of the plant contained phenols, terpens flavonoid and tannins[62-63].

Shoker found that aerial part extracts of *Convolvulus arvensis* contained terpens 3.8, alkaloids 8.90 and phenols 6.29%. The total alkaloids concentration was 1056.31 µg/ml, he isolated 8 alkaloids including Plantyneciene 211.07 Fagomine 111.82 Swainsonine 438.79 1-deoxynojirimycin 50.61, Austaline 20.10, 1-epiaustaline 59.37, 6-epicastanospermine 76.87 and Castanospermine-N- oxide 87.68 µg/ml[63].

Total phenolics and total flavonoids were determined in the acidic ethyl acetate fraction of the leaves of *Convolvulus arvensis*. Total phenolics and total flavonoids were measured as 244.6±2.9 and 174.4±0.4 mg gallic acid and rutin equivalents per gram extract, respectively[50, 64].

The qualitative and quantitative determination of polyphenolic compounds in the plant, such as coumarins and phenolic acids showed that it contained umbelliferon and scopoletin in coumarin fraction. Protocatechuic, caffeic, chlorogenic, gentisic, p-coumaric, p- hydroxybenzoic, p-hydroxyphenylacetic, ferulic, vannilic, syringic, benzoic and salicylic acids were detected in the phenolic acids fraction. Many researchers mentioned that the plant contained four coumarins, 7-hydroxycoumarin (umbelliferone); 6,7-dihydroxycoumarin (esculetin); 6-methoxy-7-hydroxycoumarin (scopoletin) and 6-methoxycoumarin7-O-glucoside (scopoletin7-O-glucoside), and eleven flavonoids including Kaempferol and its 3-O-β-D-glucoside, 7-

O-β-D-glucoside, 3-O-α-L-rhamnosyl, 7-O-β-D-glucoside, 3-O-rutinoside,7-O-rutinoside, 3-O-α-L-rhamnoside and 3-O-β-D-galactorhamnoside as well as Quercetin and its 3-O-α-L-rhamnoside and 3-O-rutinoside[50, 62, 64-66]. However, Shoker found that the plant contained 10 phenolic compounds, their total concentration was 1479.12 (µg/ml), including Caffeic acid 53.53, Thujone 197.55, Cymene 265.24, Ferulic acid 103.17, Isoferulic acid 76.77, Cimiracemoside 54.31,β-Phellandrene 368.17, Gentisic acid 191.28, Leutoline 69.32, Coumaric acid 99.78 (µg/ml)[63]. Flavonoid glycosides are well distributed in the leaves like Kaempfero l3-mono- glycosides and Quercetin 3-mono or di- glycosides[67]. Seeds from *Convolvulus arvensis* contained 6.7-16.5% oil. The chemical composition of oil consist of palmitic 6.6-10.0%, stearic 12.0-19.6%,oleic 21.6-30.0%, linoleic 27.8-41.3%, linolenic 6.0-9.2%, arachidic 3.3-6.4% and behenic acid 2.8-4.3%. It also contain steroids including Campesterol , Stigmasterol and β sitosterol[66].

Thirteen saponins were isolated and identified from *Convolvulus arvensis* [68]. Nine glycosidase activities were detected in isolated cell wall of cultured *Convolvulus arvensis* cells. Water extract contains primarily proteins and polysaccharides [69].

Pharmacological effects:

Cytotoxic effect:

A purified bindweed extract was used to inhibit the growth of tumour cells and to inhibt the growth of blood vessels and enhance immune function. The high molecular weight extract inhibited angiogenesis in chicken chorioallantoin membranes by 73% and at the dose of 14 mg inhibited tumour growth in mice by 77%[60].

The cytotoxic effects of chloroform, ethyl acetate and hydroalcoholic extracts of arial parts of *Convolvulus arvensis* were evaluated in human tumor cell line (Hela). Different concentrations of the extracts were added to the cultured cells and incubated for 72 h. Cell survival was evaluated using MTT assay. Chloroform extract showed the highest cytotoxic effect among the extracts (IC_{50} 15 µg/ml), whereas ethyl acetate and hydroalcoholic extracts were less cytotoxic against Hela cells (IC_{50} was 25 and 65µg/ml, respectively)[70]. PGM protein isolated from the water extract inhibited the tumor growth and angiogenesis in chick embryo and improved lymphocyte[60, 70-71].

The aerial parts of *Convolvulus arvensis* were extracted with 80% aqueous ethanol and fractionated using petroleum ether, chloroform, ethyl acetate and *n*-butanol which were then examined on bone marrow of mice by measuring the mitotic index (MI) and chromosomal aberrations (CA) in addition to the total white blood cells counts (WBCs) for two doses of the each fraction, 200 and 400mg/kg. The *in vitro* tests included assessment of cultured cell viability of human rabdomyosarcoma RD and human normal lymphocytes with measurement of tumor necrosis factor alpha TNF-α in cultured media using three concentrations 25µg/ml, 50µg/ml and 100µg/ml for each fraction. Results revealed that the chloroform and *n*-butanol fractions significantly decreased MI and increased CA in a dose of 200 and 400mg/kg. The petroleum ether only in high doses gave significant effects. The ethyl acetate fraction of low dose increased MI and decreased CA, while the high dose gave the inverse action. The *in vitro* study showed inhibition the viability of the cultured cell as the concentrations increased, for all the fractions accompanied with decreased the level of TNF-α[72].

The cytotoxic effect of ethanol extract of aerial parts of *Convolvulus arvensis* was evaluated against lymphoblastic leukemia, Jurkat cells. The cells were exposed to different concentrations (10, 25, 50, 75 and 100 µg/ml) of the extract to determine cell viability, cell proliferation and apoptosis using trypan blue exclusion assay, 3-(4,5- dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) and fluorescent activated cell sorter (FACS) analysis. Trypan blue exclusion assay and MTS assay results indicated that the ethanol extract decreased the number of living cells in a concentration-dependent fashion. The results of FACS analysis showed that the lowest concentration of the extract (10 µg/ml) was most effective for the induction of apoptosis as it induced maximum apoptosis (85.34 %) and the highest concentration (100 µg/ml) was less effective as it induced less apoptosis (53.70 %) in Jurkat cells ($p<0.05$)[73].

The ability of crude alkaloids extracted from the leaves of *Convolvulus arvnsis* to distract the microtubule network of mice cell line (CHO) (an invasive metastasis cell line) was evaluated. The assessment was carried out using the immunostaining technique. The extract was able to distract the microtubules of the cells line after 60 min of exposure in a concentration as little as 20 µg/ml. In DAPI staining, the cells apoptosis was not detected in this concentration. The apoptotic cell have been observed when the concentration of the alkaloid extract elevated up to 80 and 100 µg/ml. The cells were capable of recovering there native microtubules constriction after 12 hr of the alkaloid removal from the media. The extract concentration of 1mg/Kg/bw efficiently inhibited CHO cell line tumor growth to 97.14% in mice after three weeks treatment compared to untreated control animals[74].

The cytotoxicity of (aqueous and methanol) crude leaves, stems and roots extracts as well as proteoglycan and glycoside fraction I (FI) of *Convolvulus arvensis* was evaluated against human Rhabdomyosarcoma (RD) tumor cell line *in vitro*. The effect of glycoside FI fraction on mitotic index (MI) of RD cell line was investigated as well. Aqueous and methanol leaves extracts and glycoside FI had more cytotoxic effects at 10 mg/ml after 24 h. After 48 h, proteoglycan and glycoside FI at 10 mg/ml revealed very high cytotoxic activity compared with other concentrations. After 72 h, glycoside FI at 10 mg/ml showed more cytotoxic inhibition compared with other extracts. The cytotoxic concentration 50% (CC_{50}%) of Glycoside FI was 1.775, 0.870 and 0.706 mg/ml after 24, 48, and 72 h, respectively. The root aqueous extract had less cytotoxic effect after 72 h than other extracts; the CC_{50} % was 7.437 mg/ml. Cytotoxicity of root aqueous extract was more pronounced at high concentration, 10 mg/ml. The effect of glycoside FI on MI of RD tumor cell line was concentration dependant[75].

The cytotoxic effect of *Convolvulus arvensis* (methanolic extract) was evaluated against 2 stage skin carcinogenesis protocol, by tumor initiator, 7-12-dimethyl benz(a)antheracene (DMBA) and tumor promoter, croton oil in Swiss albino mice. They induced 100% skin ulceration in carcinogen control, and cumulative number of papilloma (CP), tumor yield (TY) and tumor burden (TB) were calculated as 18.20 ± 1.643, 3.640 ± 0.3286 and 3.640 ± 0.3286, respectively. Local application of the extract at 300 mg/kg/day inhibited the tumor incidence up to 20% in 16 weeks and showed a significant decline in continuous group in CP 4.800 ± 6.611 and TY 0.9600 ± 1.322 compared to carcinogen group. For assistance of morphological alteration, biochemical investigations were performed. Extract increased the reduced glutathione from 3.286 ± 0.207 to 7.1260 ± 0.4953 µmol/g, superoxide dismutase from 1.722 ± 0.1262 to 6.5160 ± 0.3710 µmol/g, catalase from 13.624 ± 0.813 to 18.792 ± 0.714 of H_2O_2 reduction/mg protein/min, and decreased lipid peroxidation from 7.652 ± 0.1863 to 4.2340 ± 0.5928 nmol/mg compared to carcinogen group. Histopathological changes showed papilomatosis and ulceration in carcinogen while acanthosis with normal psychological features in the continuous group[76].

Antioxidant effect:

The antioxidant activity of the *Convolvulus arvensis* ethanol extract has been evaluated by different ways. The antioxidant activity of the extract assessed by (ABTS) radical cation, the oxygen radical absorbance capacity (ORAC) and the ferric reducing antioxidant power (FRAP) was 1.62 mmol Trolox equivalents (TE)/g DW, 1.71 mmol TE/g DW and 2.11 mmol TE/g DW, respectively. A preliminary study of gelatine based film containing *Convolvulus arvensis* showed a strong antioxidant effect in preventing the degradation of lipid in muscle food. Accordingly, the results indicated that *Convolvulus arvensis* extract can be used as a natural food antioxidant[77].

Aerial parts of *Convolvulus arvensis* were subjected to extraction and further fractionation to obtain antioxidant rich fraction. Different concentrations of methanolic extract and its ethyl acetate fraction were subjected to antioxidant assay by DPPH method, nitric oxide scavenging activity and reducing power assay. The fractions showed dose dependent free radical scavenging property in all the models. IC_{50} values for methanolic extract and its ethyl acetate fraction were found to be 131.03 ± 2.46 and 43.21 ± 4.45 µg/ml respectively in comparison to 6.537 ± 0.235 and 5.437 ± 0.206 µg/ml for L-ascorbic acid and rutin respectively in DPPH model. In nitric oxide scavenging activity the IC_{50} values were found to be 130.12 ± 2.46 and 57.5 ± 4.45 µg/ml for methanolic extract and its ethyl acetate fraction, and 21.06 ± 0.953 and 29.93 ± 0.324 µg/ml for L-ascorbic acid and rutin respectively. The fractions showed good reducing power with increasing concentration. However, the ethyl acetate fraction showed a good reducing power and better free radical scavenging activity as compared to methanolic extract, its antioxidant potential was comparable to standards[78].

Acidic ethyl acetate fraction was prepared from the leaves of *Convolvulus arvensis*, antioxidant activity and reducing power were evaluated for this fraction. The fraction exhibited strong antioxidant activity measured by 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging method and its IC_{50} value was 66.9±0.1 pg/ml. Furthermore, it possessed strong reducing power and inhibited the oxidation of P-carotene[64].

Vasodilating effect:

Ethanolic and aqueous extract of *Convolvulus arvensis* induced vasodilatation in rabbit isolated aortic rings. The molecular level (K^+ and Ca^{+2} channels and α1 receptors) of vasodilator action of both ethanolic and aqueous extract of *Convolvulus arvensis* was studied in isolated and phenylephrine- precontracted rabbit aortic rings. The role of potassium channels was determine by using two potassium channels blockers [glibenclamide and tetraethyl ammonium (TEA)], the aortic rings were contracted by using high K^+ Krebs

solution in order to test the role of voltage gated calcium channels (VGCC). The concentration- response curves of phenylephrine in rings were carried out before and after added the two extracts in different doses to examine the role of α1 receptors. The results showed that calcium-dependent K channels (BKCa) has a partial role in the relaxing effect of the ethanolic extract, while the K^+ channels did not exhibit role in case of aqueous extract. With the using of high K^+ Krebs, both extracts exhibited relaxant effect due to reducing the entry of calcium ions from outside. The adrenergic receptor α1 has a role but with different magnitude between the extracts, with high degree for aqueous extract, that reduced the maximum response (E_{max}) of aortic rings to phenylephrine, and this was similar to the effect of α1-blocker (prazosin). Accordingly, the differences in the potency of relaxing effect gave evidence that several compounds responsible for the vasodilator effect of *Convolvulus arvensis*[79-80].

Immunostimulant effect:

Intraperitoneal injection of 1/10 LD_{50} of aqueous extract of *Convolvulus arvensis* to rats significantly increased total leukocytes and percentage lymphocyte, enhanced the phagocytic function of reticular endothelial system and blocked immunosuppressive effect produced by dexamethasone. Furthermore, the aqueous extract significantly increased the concentration of some immunomodulators such as leptin, neopterin, immunoglobulins and lysosmal enzyme activity. These results showed that the *Convolvulus arvensis* leaves contain water soluble fraction that was immunostimulant[81].

Hepatoprotective effect: The hepatoprotective activity of *Convolvulus arvensis* was studied in paracetamol-induced hepatotoxicity in mice. The results showed that ethanolic extract of *Convolvulus arvensis* (200 and 500 mg/kg) produced significant ($p<0.05$) decrease in paracetamol induced increased levels of liver enzymes and total bilirubin. Histopathological investigation supported the hepato-protective effects of *Convolvulus arvensis* [52].

Antibacterial effect: The aqueous and acetonic extracts of *Convolvulus arvensis* were tested against *Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli* and *Klebsiella pneumonia* using five concentrations (500, 250,125, 0.06 and 0.03 mg/ ml). The aqueous extract of *Convolvulus arvensis* showed no antibacterial activity against all the tested microorganisms in all concentrations. However, ethanolic extract of *Convolvulus arvensis* L. showed antibacterial activity against all the tested microorganisms (except *Klebsiella pneumonia*) when used in a concentration of 0.06 mg/ml and more[82].

Antidiarrhoeal effect: The antidiarrhoeal activity of the aerial parts methyl alcohol extracts of *Convolvulus arvensis* (200 and 400 mg/kg) was investigated in castor oil-induced diarrhea in rats, and on the motility of isolated rabbit's duodenum. Oral administration of methanol extract of *Convolvulus arvensis* in a dose of 400 mg/kg produced no significant effect on the fecal discharge in rats. On the other hand *Convolvulus arvensis* induced a dose-dependent (0.8-3.2 mg/ml) inhibitory effect on the isolated rabbit duodenum. This effect was slow in onset at small doses. Calcium chloride (25 µg/ml) added to the calcium-free solution reversed the contractile response of the rabbit's duodenum. Acetylcholine and small dose of nicotine reversed the contractile response of the tissues. Moreover, the extract produced its effect after blocking by propranolol or by yohimbine[83].

However, oral administration of 1/10 LD_{50} of alcoholic extract of *Convolvulus arvensis* blocked diarrhea, enteropooling and intestinal transits induced by castor oil in rats, comparable to that of atropine[81].

Diuretic effect:

The diuretic effect of the *Convolvulus arvensis* root extracts were assessed in rats with the using furosemide as standard diuretic drug. The parameters studied were included body weight before and after test period, total urine volume, urine concentration of Na^+, K^+ , $HCO_3^-$and Cl^-. The water and ethanol extracts (50 and 100 mg/kg) of the root extract of *Convolvulus arvensis* produced time dependent increase in urine output. Electrolyte excretion was also significantly affected by the extracts. The water extract increased the urine excretion of Na^+, K^+ and HCO_3^-. In contrast, the ethanol extract increased the excretion of HCO_3^-, decreased the loss of K^+ and had little effect on renal removal of Na^+. The high-ceiling diuretic, furosemide, increased the renal excretion of Na^+ and Cl^-; but had no effect on K^+ and HCO_3^- loss[84].

Toxicity:

Horses ingested *Convolvulus arvensis* in a few, localized northern Colorado pastures exhibited weight loss and colic. At post mortem investigation showed intestinal fibrosis and vascular sclerosis of the small intestine. *Convolvulus arvensis* of the pasture was found to contain the tropane alkaloids tropine, pseudotropine, and tropinone and the pyrrolidine alkaloids cuscohygrine and hygrine. Pseudotropine, the major alkaloid, was

known to affect motility and might represent a causative agent for the observed cases of equine intestinal fibrosis[62].

Laboratory mice readily ate *Convolvulus arvensis* exhibited a variety of abnormal clinical signs depending on the amount eaten [62].

The toxicity of *Convolvulus arvensis* was evaluated in sheep and rats. Initially sheep and rats were divided into 3 groups. One group served as controls and fed Rhodes in case of sheep and rat diet in case of rats. The other groups were fed either exclusively on binweed leaves or on 50 % binweed combined with Rhodes or rat diet. Sheep or rats either died or intoxicated by the plant, 7 days post dosing with clinical signs included dilated pupil, pale mucous membrane, respiratory distress, ataxia, convulsion and diarrhea. Macroscopic and microscopic lesions included gaseous distended intestine, congestion, oedema and hemorrhage of many organs. Decreased Hb, PCV and RBC count were suggestive of anemia. Elevation of enzymes indicating liver and kidney dysfunction. Animals fed 50 % binweed did not develop any signs of toxicity. Oral administration at a dose of 0.5 g/ rat of binweed for 10 days caused decreased protein in liver homogenate and inhibited the activity of phase-1 drug metabolizing enzymes. LD_{50} of alcoholic and aqueous fractions were 160 ± 5 mg / kg and 410 ± 6 mg / kg , respectively, suggesting that the binweed toxicity occurring in sheep and rats may possibly due to alcoholic fraction[81].

2- *Convolvulus scammonia*

Synonyms: *Convolvulus scammonia* var. *pseudoscammonia* Sa'ad[85].

Common names:

Arabic: Sigmonia, mahmoda, helablab; **English:** scammony Syrian bindweed, purging bindweed; **French:** scammonée**; German:** kleinasiatische Winde**; India:** sak munia, **Spanish**: escamonia; **Swedish**: hartsvinda[86].

Taxonomic classification:

Kingdom: Plantae; **Phylum**: Magnoliophyta; **Class**: Magnoliopsida; **Order**: Solanales; **Family**: Convolvulaceae; **Genus**: *Convolvulus*; **Species**: *Convolvulus scammonia*[87].

Distribution:

The plant was native in Asia **(**Iraq, Palestine, Jordan, Lebanon, Syria, Turkey, Iran, Syria) and Europe: (Ukraine)[86].

Description:

Convolvulus scammonia has a perennial, fleshy, fusiform root, from 3 to 5 feet long, and from 3 to 5 inches in diameter, branched toward the lower end, with a grayish bark, and abounding in an acrid, milky juice. The stems are annual, numerous, slender, round, smooth, branching, twining, very slightly angular near the ends, and growing from 12 to 20 feet upon the soil, or on adjacent plants. The leaves are on long petioles, alternate, sagittate, oblong, acute, entire, quite smooth, truncate and angular at the base, with acute, spreading lobes, and of a bright-green color. The flowers are borne on axillary, solitary, 3-flowered peduncles, scarcely twice as long as the leaves. Sepals five, rather lax, smooth, ovate, repand, obtuse, with a reflexed point, and covered at the edge. Corolla funnel-shaped, very much expanded, pale sulphur-yellow, thrice as long as the calyx, an inch or more in length; limb entire, and somewhat reflexed. Stamens five, erect, converging, thrice as short as the corolla. Ovary 2-celled, 4-seeded, supporting a slender style as long as the stamens, with 2 linear-cylindrical, erect, oblong, parallel, distant, and white stigmas. Capsule 2-celled; seeds small and pyramid-shaped [88-89].

Traditional uses:

A drink was prepared by mixing scammony and sugar in some water. This remedy was used as purgative and to expell all depositions and poisons. Repeating the therapy after one month was used to keep off fevers, shivers and quartan fevers (malaria) for the rest of the year. However, although Dioscorides was well acquainted with the purgative effects of scammony and Paulus Aegineta applied the drug in numerous simple and compound remedies for this purpose, neither of them mentioned fever or malaria. Unlike these two, the physician Alexander of Tralles from Lydia in Asia Minor, in the 6th century, highlighted the usefulness of scammony in quartan and other fevers[90].

As general, resin from rhizomes was used as hydragogue, cathartic and administered in dropsy and anascara[91].

Convolvulus scammonia was used as uterotonic and abortifacient[92], for the treatment of edema, ascites, hydroncus, simple obesity, lung fever and ardent fever[93].

Chemical constituents:

Scammony resin is prepared by exhausting scammony root by percolation with alcohol, then recovering most of the alcohol by distillation, and precipitating the resin from the residual liquid by slowly pouring it, with constant stirring, into ten times its volume of water. After the resin has subsided, it is collected on a filter, washed with boiling, distilled water, and dried on a water-bath. The resin, obtained was brownish, translucent, brittle pieces, with a sweet, fragrant odour, and resinous fracture. It consisted almost entirely of the glucosidal resin, scammonin. Boiling with a diluted mineral acid converted it into scammonolic acid and glucose. It dissolves in hot solutions of caustic alkalies, and was re-precipitated on acidifying[(94)].

The roots contain an average 8% resin together with dihydroxy cinnamic acid, beta-methyl-esculetin, ipuranol, surcose, a reducing sugar and starch. The resin consisted of the glycosides and methylpentosides of jalapinolic acid and its methyl ester[(91)].

The ether-soluble resin glycoside (jalapin) fraction obtained from scammony roots, on alkaline hydrolysis, gave a glycosidic acid, scammonic acid A, together with isobutyric, 2*S*-methylbutyric and tiglic acids. In addition, ether-soluble resin glycosides called scammonin I , II, III, IV, V, VI, VII, VIII were isolated from the root of *Convolvulus scammonia*[(95-97)].

Pharmacological effects:

Purgative effect: Scammony, gum-resin which obtained from the root of *Convolvulus scammonia* was used as a drastic purgative in 1 to 3-grain doses. In large doses it acts as a strong gastro-intestinal irritant, and may cause death, if administered to weak, debilitated persons[(98)].

The active principle of Scammony (*Convolvulus scammonia*) was inert until it has passed from the stomach into the duodenum, where it meets the bile, a chemical reaction occurring between it and the taurocholate and glycocholate of sodium, whereby it was converted into a powerful purgative[(99)].

Vasorelaxation and anti platelet aggregation effect: The effects of tincture from *Convolvulus scammonia* (200µg/ml) was evaluated on platelet aggregation. Tincture of *Convolvulus scammonia* did not show any antiplatelet effect. In the evaluation of vasorelaxant activity on rat cylindrical stripes of thoracic aorta, it also didn't show vasorelaxant activity[(100)].

Anticancer and cellular protective effect: The effect of aqueous and alkaloid crude extracts of *Convolvulus scammonia* on bone marrow cells multiplication was studied in mice implanted with hepatic cancer cells (hepatic cell H22). The inhibitory effect of crude aqueous extract of *Convolvulus scammonia* dried extracts was compared with crude alkaloidal extract, on the bone marrow cells multiplication in mice at doses of 10, 20, 40, 80 160 mg/kg. The inhibitory effects of each extract was compared with colchicine. The crude alkaloid extract showed arresting percent of metaphase more than aqueous extract in the small doses, in high doses (160 mglkg), both achieved 70% of the inhibitory effect of cholchicine. Furthermore, the study also showed that both extracts were active in reducing tumor size in dose dependent manner. The high therapeutic doses of aqueous and alkaloids extracts were 1.2 and 1 mg/kg which reduce the tumor size by 87.1 and 87.9% respectively[(101)].

The ability of crude alkaloids extracted from the leaves of *Convolvulus scammonia* was evaluated in mice hepatocarcinoma cell line (H22), which is an invasive metastasis cell line. The assessment was carried out using the immunostaining technique. The extract was able to distract the microtubules of the cells under investigation after 60 min of exposure in a concentration as little as 20 µg/ml. In using of DAPI staining, the cells apoptosis was not detected in this concentration and time. The apoptotic cell have been observed when the concentration of the alkaloid extract elevated up to 80 and 100 µg/ml during the mentioned exposure time. The cells were capable of recovering their native microtubules constriction after 12 hr of the alkaloid removal from the media. The extract concentration of 1mg/Kg bw efficiently inhibited H22 cell line tumor growth *in vivo* to 97.14% in mice after three weeks treatment compared to untreated control animals[(102)].

The effect of crude alkaloid and aqueous extraction from roots of *Convolvulus scammonia* was studied on the microtubule network of CHO cell line (China hamster). Computer-assisted image analysis model was used for demonstration the microtubule network changes induced by crude alkaloids. Cells were treated with alkaloid and aqueous extraction from roots of *Convolvulus scammonia* at various concentrations 2 µg/l to 800 µg/l for 60 min, or with crude alkaloid at a concentration of 4615 µg/l and 9230 µg/l for 60 min. Microtubules were detected by means of indirect Immunofluorescence. The damage was examined in a fluorescence microscope. On the other hand, cells were treated for 60 min with alkaloid at concentrations of 20

µg/l or 800 µg/l and the recovery process was studied in time intervals of 6, 7, 8, 9, 10 hours, or 8 and 12 hours, respectively. Differences in the arrangement of microtubules were assessed by means of quantification of the cytoskeleton changes in cells treated with alkaloid at a concentration of 20 µg/l and in untreated control cells. Untreated control cells showed a microtubule network distribution along the whole cell content. Cells exposed to alkaloid and aqueous extraction from roots of *Convolvulus scammonia* at concentrations of 2 µg/l for 60 min did not show considerable changes in the regularity of microtubules. Cells exposed to concentrations of 10 , 20, 30,40, 80, 100, 200, 400, and 800 µg/l for 60 min showed changes in the arrangement of the microtubular network. The network of cytoplasmatic microtubules at concentrations of 10, 20 µg/l was thinned down, and individual fibres had a wavelike shape. The network damage increased with the increasing concentration of extracts. The microtubules appeared more thinned down with fragmentation of fibers. At a higher concentration of 400 µg/l, sometimes blebs were formed. Cells exposed to alkaloids at concentrations of 4615 µg/l and 9230 µg/l formed paracrystals. No significant difference was detected between alkaloid and aqueous extract treated cells. When cells were exposed to alkaloid at a concentration of 20 µg/l for 2, 5, or 10 minutes, no noticeable changes occurred in the microtubule network. The 20min treatment at a concentration of 20 µg/l caused disruption of microtubules. The network was thinned down, and individual fibers had a wavelike shape. The cells exposed to alkaloid at a concentration of 800 µg/l for 5 minutes showed a severely defective microtubular network[(103)].

Side effects and toxicity:

Large doses cause acute gastro-intestinal irritation, and, if absorbed, produce cystitis and nephritis[(91)].

Doses and preparation:

Powdered root, 3 to 12 grains. Powdered resin 3 to 8 grains. Compound powder 10 to 20 grains. The dose is generally from 3 to 12 grains. Seven grains of Scammony resin gradually rubbed well up with 3 oz. milk, formed a safe purgative, to which a taste of ginger can be added. It was used as a smart purge for children, especially for those with worms[(88)].

III.CONCLUSION:

This review was designed to cover the safety and efficacy of *Convolvulus arvensis* and *Convolvulus scammonia* which are widely used in traditional medicine.

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