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ADONIS AESTIVALIS: PHARMACOLOGICAL AND TOXICOLOGICAL ACTIVITIES - A REVIEW

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ABSTRACT

Adonis aestivalis (summer pheasant's eye) is an annual plant with herbaceous growth. Although *Adonis aestivalis* has low concentrations of cardiac glycosides and it can be used therapeutically, but it remains a poisonous plant and should only be used medicinally under medical supervision. This review was designed to shed light on chemical constituents, pharmacological and toxicological effects of *Adonis aestivalis*.

Key words: Chemical constituents, pharmacology, toxicology, *Adonis aestivalis*.

INTRODUCTION

Plants have the ability to synthesize a wide variety of chemical compounds that are used to perform important biological functions, the recent reviews showed that, although plants possessed wide range of pharmacological activities and can be utilize to maintain disease-free healthy life, but they were not free from toxicity [1-76]. *Adonis aestivalis* (summer pheasant's eye) is an annual plant with herbaceous growth. Although *Adonis aestivalis* has lower concentrations of cardiac glycosides than the false hellebore (*A. vernalis*), it remains a poisonous plant and should only be used medicinally under medical supervision [77]. This review was designed to shed light on chemical constituents, pharmacological and toxicological effects of *Adonis aestivalis.*

Taxonomic classification

Kingdom: Plantae; Subkingdom: Tracheobionta; Superdivision: Spermatophyta; Division: Magnoliophyta; Class: Magnoliopsida; Subclass: Magnoliidae; Order: Ranunculales; Family: Ranunculaceae; Subfamily: Ranunculoideae Tribe: Adonideae. Genus: Adonis, Species: *Adonis aestivalis* [78-79].

Common names

Arabic: ain el deek, ain el booma, nab el jamal, English name: Summer Adonis and pheasant's eye, France: adonis d'été; Italian: adonide estiva; Portuguese: casadinhos, gotas-de-sangue; Russian: adonis letniĭ; Spanish: adonis estival, gota de sangre Swedish: sommaradonis [79-80].

Distribution

It was distributed in Europe and Mediterranean region. *Adonis* spp., including *Adonis aestivalis* (summer pheasant's eye, summer adonis) have long been utilized in European folk medicine for their cardiac-enhancing effects. Summer pheasant's eye was introduced into North America as a horticultural plant, escaped cultivation and is now naturalized in the western United States. There is concern that the plant may become better established in the western region of North America and may be more commonly found as a poisonous weed in hay. Recognition of summer Adonis or any other poisonous plant in hay is instrumental in preventing poisoning. *Adonis* spp. are members of the buttercup family (Ranunculaceae) and are considered unpalatable which is most likely the reason why reports of poisoning are rare [81]. However, the plant is distributed in Africa: Algeria; Asia: Afghanistan; Iran, Iraq, Palestine, Jordan, Lebanon, Syria, Turkey, Armenia, Azerbaijan, Georgia, Russian Federation, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, China and India; **Europe**: Austria, Czech Republic, Germany, Hungary, Poland, Slovakia, Switzerland, Russian Federation, Bosnia, Herzegovina, Bulgaria, Croatia, Greece, Italy, Macedonia; Romania; Serbia; Slovenia, France and Spain [79].

Traditional uses

Infusions of *A. aestivalis* are used as diuretic, spasmolytic, sleeping draught, and cough medicine. Species of *Adonis* are used to create medicines for stimulating heart

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function. The substance used is similar to those of Digitalis (foxglove) and are often prescribed in its place, to avoid the long-term effects of digitalis-derived drugs [77, 82].

Description

Herb, annual, taprooted. Stem 1, 20-50(-100) cm. Leaves: basal leaves 3-5 cm, similar to cauline, petiolate; cauline leaves sessile or subsessile. Leaf blade 2-3-pinnatifid. Flowers 1.5-3.5 cm diam.; sepals appressed to petals, broadly obovate, ± erose in distal 1/3, minutely ciliate, otherwise glabrous; petals 6-8, ± erect, orange [yellow, scarlet, or bright red-purple], usually with dark purple basal blotch, ± plane, 10-17 mm, ca. 1.5 times length of calyx, apex slightly erose; stamens ca. 30; anthers purple-black (olive green with age); pistils 30-40. Heads of achenes cylindric, 20-30 × 7-10mm; pedicels conspicuously exserted well beyond leaves; achenes 4-6mm, glabrous, adaxial margin with low, rounded tooth, transverse flange around middle (most pronounced abaxially), abaxial keel bearing small obtuse tooth at junction with flange; beak straight, erect, 1.5-2 mm [83].

Part used: The whole herb.

Chemical constituents

The plant contained cardenolides mainly strophanthidin aglycone [84-85]. Four cardenolides were isolated for the first time from the aerial parts of Adonis aestivalis. These compounds were identified as3-epi-periplogenin, helveticoside, strophanthidin-3-O-beta-D-digitoxosido-alpha-L-cymarosido-be ta-D-glucoside and strophanthidin-3-O-beta-D-digitoxosido-beta-D-digoxoside-bet a-D-diginosido-beta-D-glucoside [86].

Chemical investigation of the seeds of *Adonis aestivalis* has led to the isolation of a new cardenolide (3*β*,5*α*,14*β*,17*β*-tetrahydroxycard-20,22-enolide), two new glycosides , and a new strophanthidin hexaglycoside , together with a known compound, strophanthidin 3-*O*-*β*-D-glucopyranoside [87].

Carotenoids and their fatty acid esters were investigated in the petals of *Adonis aestivalis*. (3S,3'S) -astaxanthin (diester: 72.2%, monoester: 13.8%, free: 1.4%) and (3S)-adonirubin (monoester: 13.8%, free: 0.3%) were identified as the major components [88].

However Kamata *et al.*, found that the total carotenoids of the flower petal of the *Adonis aestivalis* were 1979.88 µg/g, these included β- carotene 16.43 µg/g (0.83%), 4-hydroxyechinenone 17.62 µg/g (0.89%), 3-hydroxyechinenone 33.26 µg/g (1.68%), astaxanthin diester 1525.07 µg/g (77.02%), lutein 122.37 µg/g (6.18%), adonixanthin 104.35 µg/g (5.27%), astaxanthin 66.53 µg/g (3.36%), 3,3,4,4 tetrahydroxy β- carotene 32.47 µg/g (1.64%) and unidentifined compound 61.78 µg/g (1.64 %) [89].

PHARMACOLOGICAL EFFECTS

Cardiac effects

Strophanthidin aglycone is one of several cardenolides extracted from *Adonis aestivalis*. The direct effect elicited by these compounds is similar to other cardiac glycoside-containing plants and is due to inhibition of the sodium potassium adenosine triphosphatase enzyme system pump. They increase vagal tone, which decreases the rate of sinoatrial node depolarization. In intoxication, the electro-cardiographic changes seen are include bradycardia, varying levels of atrio-ventricular block, ventricular arrhythmias, and ventricular fibrillation [90-91].

Tincture of *Adonis vernalis* is used by homeopathic physicians in patients suffering from congestive cardiac failure. Its action was very much similar to digitalis on heart. Aqueous extract of *Adonis vernalis* was found to have cardiac stimulant action on isolated heart preparations. It showed protection against heart failure produced by excessive load and high potassium concentration. Tincture of *Adonis vernalis* was found to cause cardiac depression which was not blocked by the atropine. In isolated guinea pig and rabbit auricles the drug increased the threshold of electrical stimulation. The dog blood pressure responses was varied with dose, low doses showed rise in blood pressure whereas larger doses showed fall in blood pressure [92].

Cytotoxic effects

Cardenolide compounds, isolated from the seeds of *Adonis aestivalis*, were examined for their cytotoxic activity against neoplastic HSC-2, HSC-3, HSC-4, and HL-60 cells, as well as HGF, HPLF, and HPC normal cell lines. Three of five cardenolide compounds isolated from the seeds of *Adonis aestivalis* were found to display selective cytotoxicity toward malignant tumor cell lines. Although the morphological observations of HL-60 and HSC-2 cell deaths revealed changes characteristic of apoptosis, neither DNA degradation nor activation of caspase-3 was observed. The findings demonstrated that these compounds may trigger caspase-3-independent apoptotic cell death in HL-60 and HSC-2 cells [87].

Antilithiatic activity

The antilithiatic activity of extracts of dried leaves and roots powder of *Adonis aestivalis* was proven in rat [93].

Using of *A. aestivalis* as a pigment

It was well established that certain species of Adonis flower such as *Adonis aestivalis* contained astaxanthin as a major pigment. According to Neamtu *et al.*, more than 80% of the total pigments in *Adonis aestivalis* was astaxanthin, mostly in the ester form. Their results suggested that this flower could be used for salmonids as a pigment source. The coloration of salmonids and crustaceans has become of interest in the cultivation of these species as an important factor affecting consumer acceptance [94].

The flower, *Adonis aestivalis* and its pigment extract were fed to two different sizes of rainbow trout Salmo gairdneri at a level of 10mg total pigment/100g diest. The larger fish (average weitht 400g) were fed the pigment extract for 8 weeks. In the males, carotenoids were mainly deposited in the skin and a samll amount was found in the flesh. However, in the females, a relatively high level of carotenoids was detected in the flesh. The smaller fish were fed the diets containing Adonis flower petals or its pigment extract. After two weeks of feeding, the Adonis flower group discontinued feeding activity and mortalities ensued. However, no mortalities resulted in the Adonis extract group over a three month feeding period, and a noticeable pink coloration was observed in the skin of this group [89].

Toxicity

Adonis poisoning has been reported in horses, pigs, calves, rabbits and sheep. Plants of the *Adonis* genus contain cardiac glycosides similar to the toxins present in oleander and foxglove [84-85, 95-98].

Due to natural exposure to Adonis spp, acute poisonings have been reported in horses. Clinical signs of summer adonis poisoning in horses include gastrointestinal disturbances, such as colic, hemorrhagic enteritis, diarrhea or decreased gut motility. In addition, the cardiotoxins present in *Adonis* can lead to a variety of cardiac arrhythmias and death [95].

Intoxicated horses showed gastrointestinal stasis and myocardial degeneration after ingestion of *Adonis aestivalis*-contaminated hay. Endocardial hemorrhage and gaseous distension of the gastrointestinal tract were the only necropsy findings. Microscopic examination showed scattered foci of mild, acute myocardial necrosis and neutrophilic inflammation associated with endocardial and epicardial hemorrhage. *Adonis aestivalis* was identified in the hay. Strophanthidin, the aglycone of several cardenolides present in Adonis spp., was detected by liquid chromatography-mass spectrometry in gastrointestinal contents of the intoxicated horses [95, 99-100]. *Adonis aestivalis* intoxication was also recorded in the pigs. The signs and symptoms of intoxication in pigs fed a diet containing seeds of Adonis spp were include feed refusal, vomiting, dyspnea, and death [96].

Sheep did not develop clinical signs when dosed with 1 per cent bodyweight ground adonis (estimated content 11 to 17 ppm strophanthidin) via rumen cannulas, or when dosed daily for two weeks with 0.2 per cent bodyweight adonis per day. Extensive cardiac examinations demonstrated transient cardiac functional effects. No gross or microscopic lesions were evident in the heart or any other tissues examined [85].

However, cardiovascular and toxic effects of a hydroalcoholic extract from the aerial parts of *A. aestivalis* (AAHE) were investigated in sheep and mice. Six male sheep were anesthetized with sodium pentobarbital and arterial blood pressure was measured with a transducer connected to the left femoral artery. Heart rate and electrocardiogram (ECG) were registered from lead base-apex ECG derivatives connected to a Powerlab recorder. Three successive equal doses (75 mg/kg) of the hydroalcoholic extract of *A. aestivalis* intravenously administered to anesthetized sheep. *Adonis aestivalis* extract induced a significant bradycardia and hypotension in sheep. Various ECG abnormalities in sheep included sinus arrhythmia, shortened and depressed S-T interval, and absence of P wave and flattened or inverted T wave. In addition, ventricular arrhythmias, bradyarrhythmias, atrioventricular block, ventricular premature beats, ventricular tachycardia and ventricular fibrillation have also been observed [101].

Calves fed 0.2 to 1% body weight Adonis spp daily for 4 to 5 weeks complained transient, mild cardiac abnormalities during the feeding trial. Mild, transient gastrointestinal and cardiac signs were noted in the pre-ruminating calves. No gross or microscopic lesions were seen on necropsies performed at the end of the study [79].

Microscopical examination of rabbits tissues experimently intoxicated with *A. aestivalis* showed severe hemorrhage, myocardial degeneration and necrosis in cardiac cells, severe congestion and swelling of hepatocytes in liver, spread interstitial alveolar edema, congestion of pulmonary arteries, medial hyperplasia and emphysema in lungs, PVC (pre-vascular cuffing), chromatolysis, neurophagy and focal gliosis in brain, severe swelling of tubular endothelial cells, congestion of glomeruli, hyaline casts and severe tubular necrosis in kidney, papillary hyperplasia of mucus layer, and mucous secretions into the intestine lumen were also observed [98].

In mice, the mortality rate of the intra-peritoneally administered hydroalcoholic extract from the aerial parts of *A. aestivalis* (AAHE) increased progressively with the increasing dose (data not shown): the mortality rate of 0% at and up to a dose of 1500 mg/kg gradually rose to 100% at 5000 mg/kg, the highest dose studied. The no-observed-adverse-effect level (NOAEL) for the intraperitoneal dose was 1000 mg/kg, while the lowest-observed-adverse-effect level (LOAEL) was 1600 mg/kg. The severity of clinical signs was similar appreciably between individuals. Some adverse effects, such as salivation, hypo-activity, ataxia, posterior paralysis and recumbency were seen immediately after the intraperitoneal injection, while others (decreased appetite and weight loss) were observed soon after, and were more pronounced at the higher doses. Interestingly limb paralysis that leads to recumbency was resolved spontaneously later. The acute intraperitoneal toxicity (LD_{50}) of *A. aestavalis* hydroalcoholic extract (AAHE) in mice was 2150 mg/kg [101].

CONCLUSION

This review highlight the chemical constituents, pharmacological and toxicological effects of *A. aestivalis* as a plant contains cardiovascular active metabolites.

Although, it can be used therapeutically, but it remains a poisonous plant and should only be used medicinally under medical supervision.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

1. Al-Snafi AE. Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review. *International Journal of Pharmacy and Industrial Research*, 3(3), 2013, 257-265.
2. Al-Snafi AE. Pharmacological effects of *Allium* species grown in Iraq. An overview. *International Journal of Pharmaceutical and health care Research*, 1(4), 2013, 132-147.
3. Al-Snafi AE. Chemical constituents and pharmacological activities of Milfoil (*Achillea santolina*) - A Review. *Int J Pharm Tech Res*, 5(3), 2013, 1373-1377.
4. Al-Snafi AE. The Pharmaceutical importance of *Althaea officinalis* and *Althaea rosea*: A Review. *Int J Pharm Tech Res*, 5(3), 2013, 1387-1385.
5. Al-Snafi AE. Anti-inflammatory and antibacterial activities of *Lippia nodiflora* and its effect on blood clotting time. *J Thi Qar Sci*, 4(1), 2013, 25-30.
6. Al-Snafi AE. The pharmacology of *Bacopa monniera*. A review. *International Journal of Pharma Sciences and Research*, 4(12), 2013, 154-159.
7. Al-Snafi AE. The Pharmacological importance of *Bauhinia variegata*. A Review. *Journal of Pharma Sciences and Research*, 4(12), 2013, 160-164.
8. Al-Snafi AE. The Pharmacological Importance of *Benincasa hispida*. A review. *Int Journal of Pharma Sciences and Research*, 4(12), 2013, 165-170.
9. Al-Snafi AE. The Chemical constituents and pharmacological effects of *Bryophyllum calycinum*. A review. *Journal of Pharma Sciences and Research*, 4(12), 2013, 171-176.
10. Al-Snafi AE. The pharmacological activities of *Alpinia galangal* - A review. *International Journal for Pharmaceutical Research Scholars*, 3(1-1), 2013, 607-614.
11. Al-Snafi AE. Chemical constituents and pharmacological activities of *Arachis hypogaea*. – A review. *International Journal for Pharmaceutical Research Scholars*, 3(1-1), 2013, 615-623.
12. Al-Snafi AE. The Pharmacological importance and chemical constituents of *Arctium Lappa*. A review. *International Journal for Pharmaceutical Research Scholars*, 3(1-1), 2014, 663-670.
13. Al-Snafi AE. The Pharmacology of *Apium graveolens.* - A review. *International Journal for Pharmaceutical Research Scholars*, 3(1-1), 2014, 671-677.
14. Al-Snafi AE. The pharmacology of *Anchusa italica* and *Anchusa strigosa* – A review. *International Journal of Pharmacy and Pharmaceutical Sciences*, 6(4), 2014, 7-10.
15. Al-Snafi AE. The pharmacological importance of *Anethum graveolens* – A review. *International Journal of Pharmacy and Pharmaceutical Sciences*, 6(4), 2014, 11-13.
16. Al-Snafi AE, Wajdy JM and Tayseer Ali Talab. Galactagogue action of *Nigella sativa* seeds. *IOSR Journal of Pharmacy*, 4(6), 2014, 58-61.
17. Al-Snafi AE. The chemical constituents and pharmacological effects of *Adiantum capillus-veneris* - A review. *Asian Journal of Pharmaceutical Science and Technology*, 5(2), 2015, 106-111.
18. Al-Snafi AE. The pharmacological and therapeutic importance of *Agrimonia eupatoria*- A review. *Asian Journal of Pharmaceutical Science and Technology*, 5(2), 2015, 112-117.
19. Al-Snafi AE. The chemical constituents and pharmacological effects of *Ammannia baccifera* - A review. *International Journal of Pharmacy*, 5(1), 2015, 28-32.
20. Al-Snafi AE. The chemical contents and pharmacological effects of *Anagallis arvensis* - A review. *International Journal of Pharmacy*, 5(1), 2015, 37-41.
21. Al-Snafi AE, RM Hanaon, NY Yaseen, WS Abdul alhussain. Study the anticancer activity of plant phenolic compounds. *Iraqi Journal of Cancer & Medical Genetics*, 4(2), 2011, 66-71.
22. Al-Snafi AE. The pharmacological importance of *Artemisia campestris*- A review. *Asian Journal of Pharmaceutical Research*, 5(2), 2015, 88-92.
23. Al-Snafi AE. Chemical constituents and pharmacological effects of *Asclepias curassavica* A review. *Asian Journal of Pharmaceutical Research*, 5(2), 2015, 83-87.
24. Al-Snafi AE. The pharmacological importance of *Asparagus officinalis* - A review. *Journal of Pharmaceutical Biology*, 5(2), 2015, 93-98.
25. Al-Snafi AE. The medical importance of *Betula alba* - An overview. *Journal of Pharmaceutical Biology*, 5(2), 2015, 99-103.

26. Al-Snafi AE. Bioactive components *and* pharmacological effects of *Canna indica*- An Overview. *International Journal of Pharmacology and toxicology*, 5(2), 2015, 71-75.
27. Al-Snafi AE. The chemical constituents and pharmacological effects of *Capsella bursa-pastoris* - A review. *International Journal of Pharmacology and toxicology*, 5(2), 2015, 76-81.
28. Al-Snafi AE. The pharmacological importance of *Ailanthus altissima*- A review. *International Journal of Pharmacy Review and Research*, 5(2), 2015, 121-129.
29. Al-Snafi AE. *Alhagi maurorum* as a potential medicinal herb: An Overview. *International Journal of Pharmacy Review and Research*, 5(2), 2015, 130-136.
30. Al-Snafi AE. The pharmacological importance of *Aloe vera*- A review. *International Journal of Phytopharmacy Research*, 6(1), 2015, 28-33.
31. Al-Snafi AE. The constituents and biological effects of *Arundo donax* - A review. *International Journal of Phytopharmacy Research*, 6(1), 2015, 34-40.
32. Al-Snafi AE. The nutritional and therapeutic importance of *Avena sativa* - An Overview. *International Journal of Phytotherapy*, 5(1), 2015, 48-56.
33. Al-Snafi AE. The Pharmacological importance of *Bellis perennis* - A review. *International Journal of Phytotherapy*, 5(2), 2015, 63-69.
34. Al-Snafi AE. The chemical constituents and pharmacological effects of *Capparis spinosa* - An overview. *Indian Journal of Pharmaceutical Science and Research*, 5(2), 2015, 93-100.
35. Al-Snafi AE. The chemical constituents and pharmacological effects of *Carum carvi* - A review. *Indian Journal of Pharmaceutical Science and Research*, 5(2), 2015, 72-82.
36. Al-Snafi AE. The pharmacological importance of *Casuarina equisetifolia* - An Overview. *International Journal of Pharmacological Screening Methods*, 5(1), 2015, 4-9.
37. Al-Snafi AE. The chemical constituents and pharmacological effects of *Chenopodium album* - An overview. *International J of Pharmacological Screening Methods*, 5(1), 2015, 10-17.
38. Al-Snafi AE, The effect of date palm pollens and zinc sulphate in the treatment of human male infertility. *Tikrit Journal of Pharmaceutical Sciences*, 2(1), 2006, 31-34.
39. Al–Snafi AE. Pharmacology and medicinal properties of *Caesalpinia crista* - An overview. *International Journal of Pharmacy*, 5(2), 2015, 71-83.
40. Al-Snafi AE. The chemical constituents and pharmacological effects of *Calendula officinalis* - A review. *Indian Journal of Pharmaceutical Science & Research*, 5(3), 2015, 172-185.
41. Al-Snafi AE. The constituents and pharmacological properties of *Calotropis procera* - An Overview. *International Journal of Pharmacy Review & Research*, 5(3), 2015, 259-275.
42. Al-Snafi AE. The pharmacological importance of Capsicum species (*Capsicum annuum* and *Capsicum frutescens*) grown in Iraq. *Journal of Pharmaceutical Biology*, 5(3), 124-142.
43. Al-Snafi AE. The chemical constituents and pharmacological importance of *Carthamus tinctorius* - An overview. *Journal of Pharmaceutical Biology*, 5(3), 2015, 143-166.
44. Al-Snafi AE. The therapeutic importance of *Cassia occidentalis* - An overview. *Indian Journal of Pharmaceutical Science & Research*, 5(3), 2015, 158-171.
45. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their detoxification capacity and protective effects (part 1). *Asian Journal of Pharmaceutical Science & Technology*, 5(4), 2015, 257-270.
46. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with hypolipidemic, hemostatic, fibrinolytic and anticoagulant effects (part 1). *Asian Journal of Pharmaceutical Science & Technology*, 5(4), 2015, 271-284.
47. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their effect on reproductive systems (part 1). *Ind J of Pharm Sci & Res*, 5(4), 2015, 240-248.
48. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their gastro-intestinal effects (part 1). *Ind J of Pharm Sci & Res*, 5(4), 2015, 220-232.
49. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antiparasitic, antiprotozoal, molluscicidal and insecticidal activity (part 1). *J of Pharmaceutical Biology*, 5(3), 2015, 203-217.
50. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with antidiabetic effects (part 1). *J of Pharmaceutical Biology*, 5(3), 2015, 218-229.
51. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with antifungal activity (part 1). *Int J of Pharm Rev & Res*, 5(3), 2015, 321-327.
52. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their dermatological effects (part 1). *Int J of Pharm Rev & Res*, 5(4), 2015, 328-337.
53. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with anticancer activity (part 1). *Int J of Pharmacy*, 5(3), 2015, 104-124.

54. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with anti-inflammatory, antipyretic and analgesic activity (part 1). *Int J of Pharmacy*, 5(3), 2015, 125-147.
55. Al-Snafi AE. Cardiovascular effects of *Carthamus tinctorius*: A mini-review. *Asian Journal of Pharmaceutical Research*, 5(3), 2015, 199-209.
56. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their immunological effects (part 1). *Asian Journal of Pharmaceutical Research*, 5(3), 2015, 208-216.
57. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antibacterial activity (part 1). *International Journal of Pharmacology and Toxicology*, 6(3), 2015, 137-158.
58. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with antioxidant activity (part 1). *International Journal of Pharmacology and Toxicology*, 6(3), 2015, 159-182.
59. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their respiratory effects (part 1). *International Journal of Pharmacological Screening Methods*, 5(2), 2015, 64-71.
60. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antiviral activity (part 1). *International Journal of Pharmacological Screening Methods*, 5(2), 2015, 72-79.
61. Al-Snafi AE. Galactagogue action of the crude phenolic extracts of grape seeds (*Vitis vinifera*). *International Journal of Biological & Pharmaceutical Research*, 6(8), 2015, 577-580.
62. Al-Snafi AE. Mammary gland stimulating effects of the crude phenolic extracts of green tea (*Camellia sinensis*). *International Journal of Biological & Pharmaceutical Research*, 6(7), 2015, 573-576.
63. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with cardiovascular effects (part 1). *Int J of Pharmacology & Toxicology*, 5(3), 2015, 163-176.
64. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of medicinal plants with central nervous effects (part 1). *Int J of Pharmacology & Toxicology*, 5(3), 2015, 177-192.
65. Al-Snafi AE. The pharmacological Importance of *Antirrhinum majus* - A review. *Asian J of Pharm Sci & Tech*, 5(4), 2015, 313-320.
66. Al-Snafi AE. Chemical constituents and pharmacological effects of *Astragalus hamosus* and *Astragalus tribuloides* grown in Iraq. *Asian J of Pharm Sci & Tech*, 5(4), 2015, 321-328.
67. Al-Snafi AE. The Pharmacological Importance of *Ballota nigra* –A review. *Ind J of Pharm Sci & Res*, 5(4), 2015, 249-256.
68. Al-Snafi AE. Chemical constituents and pharmacological importance of *Bidens tripartitus* - A review. *Ind J of Pharm Sci & Res*, 5(4), 2015, 257-263.
69. Al-Snafi AE. The pharmacological importance of *Brassica nigra* and *Brassica rapa* grown in Iraq. *J of Pharm Biology*, 5(4), 2015, 240-253.
70. Al-Snafi AE. The chemical constituents and pharmacological importance of *Celosia* cristata – A review. *J of Pharm Biology*, 5(4), 2015, 254-261.
71. Al-Snafi AE. The pharmacological importance of *Centaurea cyanus*- A review. *Int J of Pharm Rev & Res*, 5(4), 2015, 379-384.
72. Al-Snafi AE. The chemical constituents and pharmacological importance of *Chrozophora tinctoria*. *Int J of Pharm Rev & Res*, 5(4), 2015, 391-396.
73. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants affected smooth muscles functions (part 1). *Int J of Pharmacy*, 5(2), 2015, 90-97.
74. Al-Snafi AE. Medicinal plants with anti-urolithiatic effects (part1). *Int J of Pharmacy*, 5(2), 2015, 98-103.
75. Al-Snafi AE, Allahwerdi, IY. and Jawad IA. Using of topical 5% urtica dioica ointment in treatment of psoriasis. *European Journal of Biomedical and Pharmaceutical Sciences*, 2(4), 2015, 103-111.
76. Marbin M Ideen and Al-Snafi AE. The probable therapeutic effects of Date palm pollens in treatment of male infertility. *Tikrit Journal of Pharmaceutical Sciences*, 1(1), 2015, 30-35.
77. Vermeulen N. The complete encyclopedia of herbs. 1st ed. Lisse, The Netherlands, Rebo International, 1998, 25.
78. USDA, United States Department of Agriculture, Natural resources conservation Service, Adonis aestivalis/Plants Profile for *Adonis aestivalis*, 2014.
79. USDA, United States Department of Agriculture, Agricultural Research Service, Beltsville Area. Germplasm Resources Information Network
80. www.tela-botanica.org.
81. Burrows GE and Tyrl RJ. *Adonis* L. In: Toxic Plants of North America. 1st ed. Iowa State University Press, Ames, IA 2001, 1006-1007.
82. Al-Quran *S.* Taxonomical and pharmacological survey of therapeutic plants in Jordan. *Journal of Natural Products*, 1, 2008, 10-26.
83. Flora of North America, *Adonis aestivalis* Linnaeus, 771.
84. Woods LW, George LW, Anderson ML, Woods DM, Filigenzi MS and Puschner B. Evaluation of the toxicity of

Adonis aestivalis in calves. *J Vet Diagn Invest*, 19, 2007, 581–585.
85. Woods LW, Puschner B, Filigenzi MS, Woods DM and George LW. Evaluation of the toxicity of *Adonis aestivalis* in sheep. *Veterinary Record*, 168, 2011, 49.
86. Kopp B, Krenn L, Kubelka E and Kubelka W. Cardenolides from Adonis aestivalis. *Phytochemistry*, 31(9), 1992, 3195-3198.
87. Kubo S, Kuroda M, Matsuo Y, Masatani D, Sakagami H and Mimaki Y. New cardenolides from the seeds of *Adonis aestivalis. Chem Pharm*, 60(10), 2012, 1275–1282.
88. Maoka T, Etoh T, Kishimoto S and Sakata S. Carotenoids and their fatty acid esters in the petals of *Adonis aestivalis.* Journal of Oleo Science, 60(2), 2011, 47-52.
89. Kamata T, Neamtu G, Tanaka Y, Sameshima M, and Simpson KL. Utilization of *Adonis aestivalis* as a dietary pigment source for Rainbow Trout *Salmo gairdneri. Nippon Suisan Gakkaishi*, 56(5), 1990, 783-788.
90. Elkiey M A, Darwish SM, Abdel Wahab SM, et al. Estimation of the cardiac glycosidal contents of *Adonis autoumnalis* Linn and *Adonis dentate* Del. *Planta Med*, 15, 1997, 201–204.
91. Joubert JPJ. Cardiac glycosides. In: Toxicants of plant origin, Glycosides, ed. Cheeke PR, CRC Press, Boca Raton, 1989, 61–96.
92. Shinde S, Shastry S and Agrawal S L. Cardiovascular effects of aqueous extract of *Adonis vernalis*. IX Annual conference of IPS, 91, 76-77.
93. Parameshwar P, Rao YN, Naik, V and Reddy S H. Evaluation of antilithiatic activity of *Adonis aestivalis* Linn. In male Wister rats. *Der Pharmacia Lettre*, 3(2), 2011, 104-107.
94. Neamtu GG, Tamas V and Bodea C. Die Carotinoide aus einigen Adonis-Arten. *Rev Roum Biochem*, 3, 1960, 305-310.
95. Woods LW, Filigenzi MS, Booth MC et al. Summer pheasant's Eye (*Adonis aestivalis*) poisoning in three horses. *Vet Pathol*, 41, 2004, 215-220.
96. Davies RL and Whyte PBD. *Adonis microcarpa* (pheasants eye) toxicity in pigs fed field pea screenings. *Aust Vet J*, 66, 1989, 141-143.
97. Hurst E. Family Ranunculaceae. In: The Poison Plants of New South Wales, The Snelling Printing Works PTY. LTD, Sidney, Australia, 1942, 113-114.
98. Hobbenaghi R, Javanbakht J, Kamrani M, Dezfouli A B, Hassan M A and Zamani-ahmad mahmudi, M. Histopathological study of acute toxicity of *Adonis aestivalis* (Summer Pheasant's Eye) in rabbits. *J Clin Exp Pathol*, 2, 2012, 124-128.
99. Degen A V. Adonis-vergiftung. *Fortschr Landwirtsch*, 7, 1932, 556.
100. Kummer DH. Vergiftungen bei pferden durch Adonis in luzerneheu (poisonings in horses with Adonis-contaminated alfalfa hay). *Tierarztl Umsch*, 7, 1952, 430–431.
101. Maham M and Sarrafzadeh-Rezaei F. Cardiovascular effects of *Adonis aestivalis* in anesthetized sheep. *Veterinary Research Forum*, 5(3), 2014, 193-199.