Prangos platychlaena: State of the Art from Ethnopharmacology, Phytochemical, Toxicological and Pharmacological Perspective

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Abstract: The Mediterranean region is a rich source of bioactive phytochemicals contained in plants and the secret of longevity. Mediterranean region represents an intangible cultural heritage of humanity and it is partially still based upon many wild plants. The use of wild plants possibly emerged in the Neolithic period in the Fertile Crescent and migrated westwards through the Mediterranean area. The genus of *Prangos* has 30 species distributed from the Mediterranean to central Asia, 14 of them are found in Turkey while 7 of them are found in the different areas of the Kurdistan region of Iraq. *Prangos platychlaena* Boiss. (family: Apiaceae) abundantly found in the mountains of Halgurd. *P. platychlaena* has been reported as potent antioxidant plant, and traditionally used as carminative, and diuretic. *Prangos* also traditionally used in the treatment of burning and wounds, kidney, and urinary disorders. *P. platychlaena* have been reported to cause toxicological effects in animals, and shows potential cytotoxic activities in *in-vitro* studies. The current review has covered comprehensively habitats, ethnopharmacology, phytochemistry, toxicological and pharmacological actions of *P. platychlaena*.

Keywords: *Prangos, P. Platychlaena,* Apiaceae, Traditional Uses, Cytotoxic Actions, Phytochemistry

1. Introduction

Kurdistan region of Iraq is well known for its flora, the diversity of wild plants and their natural products, which have been used for a long time by its habitants as fodder, traditional medicine and other purposes (Hamad, Balzter, & Kolo, 2017). Nowadays, the chemical compounds have been identified in plants used as new medicines and may be assumed as therapies for treating many diseases with few side effects (Hussain & Osw, 2020; Kafash-Farkhad, Asadi-Samani, & Rafieian-Kopaei, 2013). The family of Apiaceae is regarded as one of the important families, with its different species. The genus of *Prangos* belongs to the family of Apiaceae, and having 30 species distributed from the Mediterranean to central Asia (Brusotti et al., 2013), 14 of them are found in Turkey, while 7 of them are found in the different area of Kurdistan region of Iraq, and these are *P. platychlaena* Boiss., *P. ferulacea* (L.), *P. uloptera* DC., *P. asperula* Boiss., *P. pabularia* Lindl., *P. peucedanifolia* Fenz, and *P. carymbosa* Boiss (Ahmed, Guvenc, Kucukboyaci, Baldemir, & Coskun, 2011).

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Prangos platychlaena Boiss. (Family: Apiaceae) is abundantly found throughout Kurdistan and locally known as Karkul in Kurdish and Korkor or Kirkor in Turkish (Mottaghipisheh et al., 2020). The *P. platychlaena* is a perennial plant, its length can reach up to (1-1.5 m), naturally growing in the high mountains in the Kurdistan region of Iraq, on rocky slopes at the altitude of 2200-2800 m above sea level.

Their species are distributed in Halgurd mountain (Ghazanfar & Edmondson, 2013). Generally, the amount of toxicants that cause the pathogenicity or death of any organism, are correlated to the environmental factors quantitatively having effects on the plant metabolic processes and their phytochemical compounds, through their effects on the growth rate, plant development and partitioning of the assimilate into vital metabolites. These factors were temperature, moisture, light, etc. and edaphic factor such as soil nutrition, soil moisture, etc. which causes to change the qualitative and quantitative phytochemicals production (Ncube, Finnie, & Van Staden, 2012). Many factors such as age, sex, body weight, rate absorption, metabolism, genetic characteristic, the dose of toxin, toxin distribution, etc. have a great role in the toxicity assay (Hunter & Smeets, 1977).

The *P. platychlaena* Boiss. fruit contains different quantities of essential oils and other phytochemical compounds which plays an important role in biological activities (Uzel, Dirmenci, Celik, & Arabaci, 2006). In the eastern part of Turkey, several researchers reported that the *P. platychlaena* has been used as a traditional medicine to treat of wounds of cattle and for its repellent activity against mosquitos (Tabanca et al., 2018; Ulubelen et al., 1995). The present review comprehensively summarizes the habitat, morphology, ethnopharmacology, phytochemistry, toxicological effects and pharmacological actions of genus *Prangos* with special reference to *P. platychlaena* Boiss.

2. Habitat

According to (Ulubelen et al., 1995), the P. platychlaena Boiss is an endemic perennial herbaceous plant in eastern Turkey. Based on the documented information from the flora of Iraq, this plant is distributed in Iran, Palestine and Turkey. The P. platychlaena plant is found in the high mountains in the Kurdistan region of Iraq, on rocky slopes at the altitude of 2200-2800 m above sea level, the species were distributed in Halgurd, Qandil, NE of Rania (Ghazanfar & Edmondson, 2013).

3. Morphological Features

P. platychlaena is a perennial plant, length reach to 1-1.5 m, leaves pinnately decomposite into linear to filiform segments, stem and branches purplish. Inflorescence polygamous, terminal umble hermaphrodite and male, flowers are yellow, flower ± 4 mm, fruit ovoid, as shown in Figure 1 (Ghazanfar & Edmondson, 2013).

4. Taxonomic Classification

Kingdom: Plantae

Division: Tracheophyta (vascular plant)

Class: Monocotyledon

Order: Apiale

Family: Apiaceae

Genus: Prangos

Species: platychlaena

(Ghazanfar & Edmondson, 2013).

Figure 1: Morphological features of *P. platychlaena*, aerial parts and roots

5. Ethnopharmacology

Investigations on the traditional use of Prangos were recognized as a way to know and learn about potential future medicines. It is well-known that many wild plants are the source of vitamins, minerals, fiber and different types of phytochemicals. The particular plant was popular at present, since its ingredients may not only regulate body homeostasis but also prevent several diseases (James, 2014; Sarker & Nahar, 2004). In Uzbekistan, the aerial parts of P. tschimganica were used in folk medicine for skin conditions, such as leukoplakic disease (Shikishima et al., 2001). Plants have an important role in the management and treatment of wounds. Different types and large numbers of plants have been used by folklore and tribal in many countries for the treatment of burning and wounds. The presence of various health-sustaining constituents in plants has attracted scientists to examine these plants to determine potential wound healing properties (Nayak & Pinto Pereira, 2006).

As well as, before flowering time, aerial parts of the P. ferulacea (L) were put in cheese and other dairy products to provide a nice smell (Çoruh, Celep, & Özgökçe, 2007). In the Indian system of medicine, the fruit of P. pabularia is used as carminative and possesses diuretic properties, while the root in combination with Terminalia chebula, used orally in the form of tablets against all the kinds of kidney and urinary disorder, bleeding and inflammation in the kidney (Sharma, Ashok, Negi, & B, 2013). In the northern west of Iran, the plants of Prangos genus have been used as a tonic, wound healing, carminative, etc, in traditional medicine. Depending on the literature, the oil exudate of the fresh root of P. ferulacea has been used as a topical ointment as an effective wound healing agent especially for pus-filled wounds in humans (Yousefi et al., 2017).

6. Phytochemistry

The previous study demonstrated that the chromatographic separation of chloromethane extracts of P. platychlaena plant yielded different compounds, such as oxypeucedanin, heraclinin, n-butylbergaptol, lmperatorin, isoimperatorin, aeetyloxypeucedanin, prangenin and bergaptol (Ulubelen et al., 1995).

Uzel et al. (2006) revealed that the chemical analysis of fruits essential oils of P. platychlaena. The GC and GC/MS, study showed that the fruit part containing major components such as α-pinene (69.75%), β-phellandrene (10.58%), d-3-carene (3.39%) and p-cymene (3.38%). The chemical investigation of the P. platychlaena reported that the 3,5-nonadiyne, (Z)-3,5-nonadiyne-7-ene and (E)-3,5-nonadiyne-7ene were isolated from the fruits of P. platychlaena, by using column chromatography technique, and some major essential oils compounds such as α-pinene, α-phellandrene, and β-phellandrene (4.2% and 22.4%) were identified from the fruits by using GC/MS (Tabanca et al., 2018).

Rahman et al. (2020a) studied the essential oil composition of different parts (leaves, stem and flower) by GC/MS. The study shows the presence of (E)-β-ocimene (25.93%), bornyl acetate (24.58%) and α-pinene (5.84%) in leaves; bornyl acetate (25.49%), (E)-β-ocimene (22.94%) and α-pinene (9.5%) in the stem, and while in the flowers (E)-β-ocimene (28.5%), bornyl acetate (24.18%) and γ-terpinene (14.15%) as major compounds in P. platychlaena. These data indicated that the P. platychlaena containing in larger amount of each of β-ocimene, bornyl acetate, γ-terpinene and α-pinene. GC-MS analysis of essential oils from leaves and flowers of P. peucedanifolia yielded β-pinene (35.58%), α-pinene (22.13%), and β-phelandrene (35.58%) as major constituents (Brusotti et al., 2013).

In another phytochemical study on dried flowers of P. platychlaena by Rahman et al. (2020b), the authors used petroleum ether and ethanol extracts for further isolation of chemical compounds. The petroleum ether extract yielded isolation and characterization of 5,8-dimethoxy psoralen, while the ethanol fraction yielded 5-methoxy psoralen and 8-methoxy psoralen. The structures of the isolated compounds were determined by data of FT-IR, 1H-NMR, 13C-NMR, COSY, and MS spectrum. In figure 2 the structure of major chemical compounds of P. platychlaena is given.

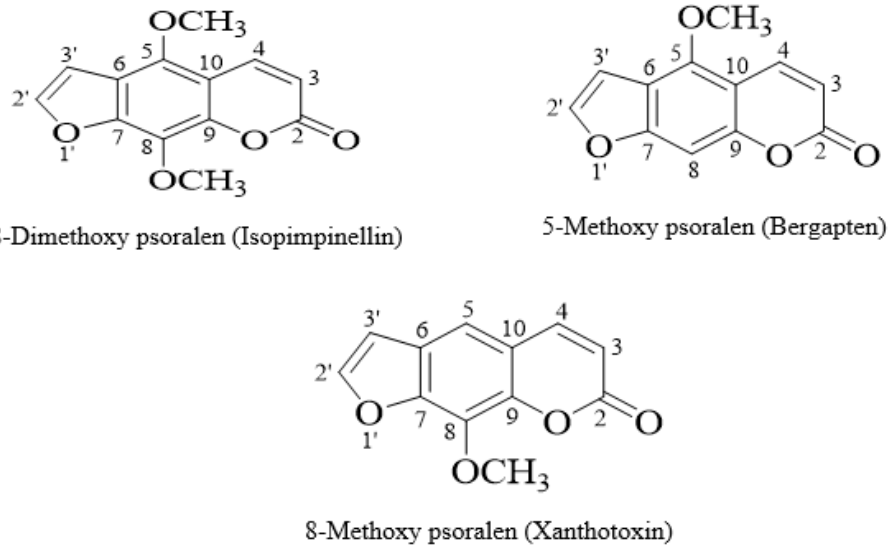

Figure 2: Chemical structure of major phytochemicals of *P. platychlaena*

7. Toxicological Effects

7.1 Toxicity of Prangos towards Other Plants

In nature, plants live in communities made up of one or more species that communicate through a variety of complex mechanisms. The plant releases many bioactive chemicals into its surrounding environment through different mechanisms from its various parts such as root, stem leaves and flowers.

These bioactive chemicals are often referred to as allelochemicals because they communicate with the surrounding environment (Mondal, Asaduzzaman, & Asao, 2015). Allelopathy is a mechanism in which chemicals produced by plants and released into the environment, which may increase or decrease the associated plant growth. The harmful effects of allelochemicals substances included: inhibition and delays of germination, deformation of seedling, the effect on physiological process such as photosynthesis and respiration which occur in the plant, stem development and swelling or decreasing in total dry matter. The allelochemicals are released into the environments through different ways such as volatilization, the decay of tissue, leaching and exudation (Rice, 1984). According to (Razavi, 2012), at the flowering stage, the leaf extracted oil of P. ferulacea prevent the root growth of lettuce with an IC50 value of 244.19mg/ml, the potential of leaf extracted oil from this species was dependent on the presence of Spathulenol and bisabolol that compose the main fractions of the oil. Accordingly, the oil can be used for the control of weeds as a bioherbicide.

7.2 Toxicity of Prangos towards Animals

Toxicity is the degree to which the substance can harm animals and refers to cell, organ or whole organism effects. Depending on quantity, all substances are potentially toxic. The principle of toxicity testing is not only to examine how safe a test substance, but also to characterize the potentially toxic effects which can be produced. Toxicity testing used a wide range of tests in the various animal species with long-term drug administration, regular monitoring of physiological, biochemical abnormalities and histological abnormalities (Arome & Chinedu, 2013). The lethal dose (LD50) calculation (the dose that kills 50 percent of the test animal population) has now been used as a significant factor in toxicity estimation and as an initial method for the general testing of chemical and pharmacological toxicity agents. There are also other biological factors, including death, and the starting date, time and degree of survival recovery are important in toxicity evaluation (Chinedu, Arome, & Ameh, 2013). According to (Hilan, Bouaoun, Aoun, Sfeir, & Garabeth, 2009), the value of LD50 in relation to the concentration of injected essential oil of P. asperula, was analyzed from the straight line defining the death rate, which was approximately 1,05 µL/g. While, the LD50 of the Osthole (7-methoxy-8-(3-methyl-2-butenyl)-2H-1-benzopyran-2-one) was 710 mg/kg, which isolated from the root of Prangos ferulacea (Yalda Shokoohinia et al., 2017).

Rahman and Jaff, (2020c), studied phytochemical, physiochemical contents and toxicity of P. platychlaena growing in Halgurd mountain of Iraqi Kurdistan. The study showed that the phytochemical contents are more concentrated in the initial growth stage than the other stages and the phytochemical concentration positively correlated with temperature and negatively correlated with humidity. The physiochemical contents such as total carbohydrate, protein, coumarin and dry weight are more concentrated in the leaves and flowers than other parts. The toxicity study revealed that the leaves cause toxicity in rats and its lethal dose was 3.95 g/kg and this is possibly due to the high quantity of coumarin in the leaves compared to other aerial parts.

7.3 Toxicity of Prangos towards Microorganisms

In hostile words, pathogens can be identified as invaders attacking host species (human). The pathogen is a micro-organism such as bacteria and fungi (yeast) that can cause diseases. Pathogenicity is also the ability of a microorganism to cause disease. There is a wide range of microorganisms that can cause serious bodily harm and become lethal. Despite the remarkable research and development of treatment and prevention procedures, infectious disease remains the main cause of the disease . Although a wide range of hosts can be attacked by many, others are specific to one host. A human

body is a preferred host for a wide range of pathogens as it provides a nutrient, warm and moist environment (Sarmah, Dan, Adapa, & TK, 2018). One person out of 10 will be ill, according to the World Health Organization, and 420,000 people die each year as a result of eating contaminated food with microbes (Pigłowski, 2019). The majority of infectious diseases in healthy people are responsible for a limited number of bacterial species such as Pseudomonas aeruginosa, Staphylococcus aureus that causes urinary tract infection, skin disease and lung disease, respectively (Alhazmi, 2015). As well Candida species such as Candida albicans, Candida glabrata and Candida parapsilosis are major human fungal pathogens that cause a mucosal oral cavity, gastrointestinal tract and vagina infections (Sardi, Scorzoni, Bernardi, Fusco-Almeida, & Mendes Giannini, 2013).

It was reported that the essential oils from the fruits of P. ferulacea showed antibacterial activity against Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa (Massumia, Fazelib, Alavic, & Ajanid, 2007). Other studies revealed the methanol extract of P. acaulis root has potent antibacterial activity against Streptococcus mutant (Nosrati, Behbahani, Mohabatkar, & Shakeran, 2018).

8. Pharmacological Actions

8.1 Anticancer Activity

Cytotoxicity studies are one of the important indicators for determining the potential toxicity of a test plant extract and active compounds isolated from plants by using the cell in vitro to observe the growth of cell. The furanocoumarins compounds such as aviprin and aviprin-3"-O-D-glucopyranoside were isolated from methanol root extract of P. uloptera, which treating the prostate human carcinoma with various concentration of the viprin and aviprin-3"- O-D-glucopyranoside showed that IC50 of aviprin and aviprin-300-O-D-glucopyranoside were 0.4 and 6.6mg/ml, respectively (Zahri, Razavi, & Moatamed, 2012).

Also, other literature survey revealed the acetone root extract of P. ferulacea provided different coumarin compounds, one of them was Osthole, which showed the cytotoxicity effect on the human ovarian carcinoma (Y. Shokoohinia, Sajjadi, Gholamzadeh, Fattahi, & Behbahani, 2014). According to (Farooq et al., 2014), the phytochemical analysis of methanol: dichloromethane (1:1) root extract of P. pabularia led to isolation of osthol compound, which have potential of cytotoxicity against epidermoid carcinoma (A431), melanoma (A375), lung (NCI-H322), lung (A549), prostate (PC-3) and colon (HCT-116) cell lines, with IC 50 values of 3.2, 6.2, 10.9, 14.5, 24.8, and 30.2 mM, respectively. Another studies revealed that the 8-methoxy psoralen have cytotoxicity potential against Hela cervical cancer cell line (Abdel Hafez et al., 2009). As well as, other worker demonstrated that the 8-methoxy psoralen, 5-methoxy psoralen and 5,8-dimethoxy psoralen were therapeutic substances with anticancer activities in human leukemia cells (Kubrak et al., 2019).

8.2 Antioxidant Activity

Free radicals have important roles in the pathogenesis of many diseases such as cancer etc. The free radicals that occur during normal body functions accelerate aging by damaging the cells and the immune system. Antioxidant constituents of the material act as radical scavengers, and helps in converting the radicals to less reactive species which reduce the most possible damage and have an important role in the prevention of human diseases. The DPPH assay was used in many studies to determine the antioxidant activities (Aruoma, 2003; Shivembe & Ojinnaka, 2017). Studies conducted in previous years (Çoruh et al., 2007) have shown P. ferulacea extracts have antioxidant properties

with an IC50 value of 0.24 mg/ml. As well as, it has been reported (Ahmed et al., 2011) that the water extracts of P. ferulacea, P. heyniae, P. meliocarpoides and P. uechtritzii display low antioxidant activities than the methanol extract of Prangos. Also, slightly antioxidant activity was observed in the fruit of P. ferulacea (Cesur, Coşge Şenkal, Yaman, Uskutoğlu, & Koç, 2017).

9. Conclusions

The wild species of Prangos abundantly growing in Iraqi Kurdistan. Prangos platychlaena Boiss., is a native plant of Kurdistan region, Iraq. P. platychlaena traditionally used for the treatment of several human ailments in Kurdish society. The current review reveals that it contains monoterpenes, sesquiterpenes and coumarins as major phytochemicals. Prangos species has been reported as potent antioxidant and anticancer plant. Prangos also known for its potent toxic actions against animals, and micro-organism. Hence Prangos plant can be a potential candidate in discovery of phytochemicals with anticancer, antimicrobial and antifungal activities.

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