Review Article

Chemical constituents and pharmacological importance of Agropyron repens – A review

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1. Introduction

Different societies use plants according to their own beliefs, knowledge, and previous experiences. Recent reviews showed that the plants are rich source of a lot of secondary metabolites which possessed a wide range of pharmacological and therapeutic effect [1-76]. Agropyron repens is native from temperate Europe to Central Asia and is now found in Africa. It is used traditionally as soothing diuretic and for calming pain and spasms in the urinary tract. It is also used as demulcent and tonic. The plant contained carbohydrates, mucilaginous substances, pectin, trititin, cyanogenetic glycosides, phenol compounds, flavonoids, saponins, volatile oils, essential oil, vanillin glucoside, iron and other minerals, and large quantities of silica. It possessed hypoglycemic, hypolipidemic, anti-inflammatory and diuretic effects. It was also affected motility, cured urinary tract infection and induced many other effects. This review will highlight the chemical constituents and pharmacological effects of Agropyron repens.

2. Plant Profile

2.1 Synonyms:
Agropyron firmum J. Presl, Agropyron repens (L) P. Beauv., Elytrigia repens (L) Desv. ex Nevski, Triticum firmum (J. Presl) Link, Triticum repens L [77].

2.2 Taxonomic classification:
Kingdom: Plantae; Subkingdom: Tracheobionta; Superdivision: Spermatophyta; Division: Magnoliophyta; Class: Liliopsida; Subclass: Commelinidae; Order: Cyperales; Family: Poaceae / Gramineae; Genus: Elymus L; Species: Elymus repens (L) [78].

2.3 Common names:
Arabic: najed, echresh, najim; Deutsch: queckenwurzelstock; English: couch grass, couch, dog grass, quack grass, quick grass, scotch, twitch grass; French: chiendent, chiendent rampant, petit chiendent; German: ackerquecke, quecke; Portugués: Grama francesa, rizoma; Spanish: grama canina; Italian: gramigna rizoma [77,79].

2.4 Distribution
It is native from temperate Europe to Central Asia and is now found in Africa: Algeria, Morocco and Tunisia; Asia: Afghanistan, Cyprus, Iran; Iraq, Lebanon, Syria, Turkey, Armenia, Azerbaijan, Georgia, Russian Federation, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, Mongolia, China, Korea, India and Pakistan; Europe: Denmark, Finland, Iceland, Ireland, Norway, Sweden, United Kingdom, Austria, Belgium, Czech Republic, Germany, Hungary, Netherlands, Poland, Switzerland, Belarus, Estonia, Latvia, Lithuania, Moldova, Russian Federation- European part, Ukraine, Albania, Bulgaria, Croatia, Greece, Italy, Romania, Serbia, Slovenia, France and Spain. It introduced in wide areas in the world as a contaminant in hay or straw. Quackgrass has now been reported from every state in the United States and throughout Canada. This invasive grass is found in both natural grassland communities and agricultural fields. It invades gardens, lawns, roadsides, ditches, and other moist areas [77,80].

2.5 Traditional uses: [1-4]
Agropyron repens is used as soothing diuretic and for calming pain and spasms in the urinary tract. It is also used as demulcent and tonic. It is widely used in children's conditions associated with urinary system (e.g. enuresis and urinary incontinence), for the control of symptoms of urinary disease, prostatic disease, rheumatism, urinary calculi and urinary infections (cystitis, urethritis, prostatitis) [80-87].

2.6 Description
Quackgrass is a strongly rhizomatous perennial plant. The rhizomes are long, highly branched, yellowish-white, sharp-pointed, and somewhat fleshy. Stems are erect and usually 1–3 feet tall. Leaf blades are ¾–1½ of an inch wide, flat at, and pointed and have small auricles at the junction of blade and sheath. Leaf blades often have a diagnostic slight constriction near the tip and are sparsely hairy above and hairs below. Spikelets are arranged in two long rows and borne flatwise to the stem. The florets are awnless to short-awned. Seeds are elliptical and pale yellow to brown [88-89].

2.7 Part used: Rhizome, mot and seeds

2.8 Chemical constituents:
The plant contained carbohydrates (fructose, glucose, inositol, mannitol), mucilaginous substances (10%), pectin, trititin, cyanogenetic glycosides, flavonoids, saponins, volatile oils 0.05%, essential oil (0.01-0.02%), 25% monoterpenes (carvacrol, carvon, trans-anethole, thymol and menthol, among others) and 0.85% sesquiterpenes, 25% monoterpenes (carvacrol, carvon, trans-anethole, thymol and menthol, among others) and 0.85% sesquiterpenes. Other constituents included vanillin glucoside, iron and other minerals, and large quantities of silica [84-86, 90-92].

Phenol compounds found in the plant were included: P-hydroxybenzoic, vanillic and p-coumaric acids, Chlorogenic acid, p-hydroxycinnamic acids, P-hydroxycinnamic acid esters: (E)- and (Z)-.
p-coumaric acid hexadecyl ester and (E)- and (Z)-p-coumaric acid-16-hydroxyhexadecylester and bis-(E)- and bis-(Z)-diesters of analogous structure [93-96].

Quack Grass seed contained oil 12%, triticin, mucilage 10%, saponins, sugar alcohols (mannitol, inositol, 2% to 3%), essential oil with polyacetylenes or carvone (0.01% to 0.05%) small amounts of vanillolide (vanillin monogluco side), vanillin, and phenolcarboxylic acids, silic acid and silicates [97].

As a nutritive value, Agropyron repens contained: dry matter 95%, organic matter 88.7%, crude protein 8.9%, crude fiber 34.3%, ether extract 1.44%, ash 11.2%, non fibrous carbohydrates 8.96%, neutral detergent fiber 69%, acid detergent fiber 38.3%, hemicelluloses 31.1%, acid detergent lignin 5.7%, acid insoluble ash 1.15%, liquefaction index 8.1, Gross energy (Kcal / Kg) 4285.1 [86].

Allelopathic constituents of ethylacetate extracts from shoots and root exudates of 10-day old Agropyron repens seedlings were investigated. The allelochemicals identified in shoot extracts included the cyclic hydroxamic acids 2,4-dihydroxy-7-methoxy-2H-1,4-benzoazin-3-one (DIMBOA) and 2,4-dihydroxy-2H-1,4-benzoazin-3-one (DIBOA), as well as the corresponding lactam derivative 2-hydroxy-1,4-benzoazin-3-one (HBOA). The concentration of major component DIMBOA was 0.5 mg/g fresh weight, the concentration of DIBOA was 0.02 mg/g fresh weight. Futhermore maleic, t-aconitic and citric acid were found. In order to estimate the allelopathic potential of living plants an investigation of root exudates was performed. The cyclic hydroxamic acids were identified as important constituents. Their concentrations were 0.4 μmol/l DIMBOA and 0.2 μmol/l DIBOA. Additionally 2,4-dihydroxy-7,β-dimethoxy-2H-1,4-benzoazin-3-one (DIM2BOA) was detected. Vanillic, fericul, and β-hydroxybutyric acid are also phytotoxins released by intact, living quackgrass seedlings [98].

3. Pharmacological effects

3.1 Hypoglycemic effects

The hypoglycemic effect of an aqueous extract of Agropyron repens (Triticum repens) rhizomes was investigated in normal and streptozotocin (STZ) diabetic rats. After a single oral administration of the aqueous extract (20mg/kg) a significant decrease on blood glucose levels in STZ diabetic rats (p<0.001) was observed; the blood glucose levels were normalized after 2 weeks of daily oral administration of aqueous extract (20mg/kg) (p<0.001).

Significant reduction on blood glucose levels were noticed in normal rats after both acute (p<0.001) and chronic treatment (p<0.001). In addition, no changes were observed in basal plasma insulin concentrations after treatment in either normal or STZ diabetic rats indicating that the underlying mechanism of this pharmacological activity seems to be independent of insulin secretion [99].

3.2 Hypolipidemic effects

The effect of single and repeated oral administration of the lyophilized aqueous extract of rhizomes of Agropyron repens (20 mg/kg) on lipid metabolism was studied in normal and streptozotocin-induced diabetic rats. In normal rats, the aqueous extract induced a significant decrease in the plasma triglycerides concentrations 4 days and 1 week after repeated oral administration. This reduction was abolished 2 weeks after once daily repeated oral administration. A significant decrease of plasma cholesterol levels was observed only 1 week after repeated oral administration. In diabetic rats, the treatment caused a significant decrease in plasma cholesterol after a single and repeated oral administration. A strong decrease in cholesterol levels was observed 6 hours after a single oral administration of the extract. Four days after the repeated oral administration of the extract, the plasma cholesterol level was significantly decreased and remained still diminished after 2 weeks. Repeated oral administration of the aqueous extract of Agropyron repens rhizome caused a significant decrease in body weight 2 weeks after oral treatment. In severely hyperglycaemic rats, Agropyron repens extract treatment induced reduction of lipid levels and body weight [100].

3.3 Effects on Motility

Experiments were performed on rota-rod with male mice (20-30 g body weight). Each group of mice (N=30) received either orally or i.p. 10% infusion of Rhizoma graminis (either 40 or 80 mg/20 g mouse). Motility tests were performed 2 and 8 hours after administration of the tested solutions. The tested plant products induced comparable significant dose-dependent inhibition of motility [101].

3.4 Anti-inflammatory

Oral administration of 80% ethanol extract of rhizomes of Agropyron repens (100 mg/kg) induced moderate inhibition of carrageenan foot oedema of the rat hind-paw (14%) compared to indomethacin (45% of inhibition) at 5 mg/kg [102].

The cream containing dry couch grass extract was tested in allergic contact dermatitis induced topically in rats after depilation with two applications of 0.1 ml of 5% alcoholic solution 2,4-dinitrochlorobenzene (DNCB). After DNCB use, the skin was hyperaemic, oedematous with serious purulent changes and itching. Couch grass extract cream was applied 3 days after the beginning of sensitization. The anti-inflammatory activity of the cream was monitored 4, 6 and 10 days after the bigning of the experiment. Plasma lipid peroxidation parameters malondialdehyde (MDA), diene conjugates (DC) and catalase activity were evaluated. After 2 days of treatment (4th day of the experiment) with couch grass cream, a decrease of erythema, oedema and infiltration was recorded. On the 6th day of the experiment, the skin of rats treated with the cream containing couch grass returned to baseline values with a reduction of oedema and erythema. The activity of catalase was increased by 30% at the 4th day and by 15% at the 6th day of the experiment, compared to the control. At the end of the experiment on the 10th day, the activity of MDA was within the control limit with an increase in the activity of catalase. The couch grass cream application quickened the recovery by 4-5 days as compared with untreated control animals. The anti-inflammatory effects of the couch grass cream were comparable to the standard glucocorticoid cream activity [93].

3.5 Diuresis and treatment of urinary tract infections:

The sugar mannitol present in large quantities in this herb, and is known as a standard ‘osmotic diuretic’, that is, it is absorbed whole from the gut and excreted largely by the kidney tubules. Its presence in the tubules means that extra water has to be retained in order to maintain osmotic pressure. The saponins and vanillin, also have diuretic properties. Because of Couch grass diuretic and antimicrobial effects, it was used to flush out the urinary tract during infections [103].

A post-marketing surveillance was designed to investigate the efficacy and tolerability of a fluid extract of Agropyron repens (Elymus repens) [Acorus drops] in patients with urinary tract infections or irritable bladder. Data for 313 patients with urinary tract infections or irritative bladder were analysed. The patients were treated on average for twelve days with 50-60 drops 3 times a day. The primary efficacy criterion was the change of urological symptoms during the course of therapy. Between 69% and 91% of the urological symptoms initially documented were relieved in the course of therapy. Depending on the underlying urological diagnosis, between 32% and 53% of the patients were completely free of symptoms following treatment. Acorus drops were tolerated very well. No adverse drug reactions occurred [104].

In an open clinical trial in 99 patients with micturition disorders (12 female and 87 male), a 20% ethanol fluid extract of Agropyron repens was administered for 28-31 days (60 drops 3 times daily). The complaints of urge incontinence, dysuria, nocturia and tenesmus due to adenoma of prostate, prostatitis and cystitis were significantly reduced in 44.4-100% of patients. Laboratory markers of inflammation (protein, epithelia, leukocytes and erythrocytes in urine) were also normalized. 96% of patients

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mentioned that the treatment is good or very good. Adverse effects were not recorded [100].

3.6 Other pharmacological effects:
Quackgrass, which is rich in silica, potassium and other minerals, has always been used as a natural medicine. During the food shortages of the First World War, bread made from quackgrass was popular in southern Germany. The seeds as well as the rhizomes were used to produce a nutritious flour to replace wheat and other grains [105].

A product named Tritipalm represents a combination of 60 grains of the fresh root of triticum and 30 grains of the fresh fruit of saw palmetto (Serenoa serrulata), in each fluid drachm. It is designed as a general nutritive tonic and sedative to irritated and inflamed states of the mucous membranes of nose, throat, and bronchia, especially arresting purulent discharges; it also acts upon the glandular appendages of the reproductive tract. It is specially recommended in nephritis, simple and gonorrheal urethritis, cystitis, vesical irritability, strangury, dysuria, and atrophy of the mammae, testes, ovaries, uterus, and especially of the prostate gland. The dose is 1 fluid drachm, followed by a draught of water, 4 times a day [103].

However, Grasses et al., found that Agropyron repens L. exerted no effect on urolithiasis risk factors when given to the rats in combination with different diets (standard, high glucidic and high protein) [106].

It was one of the medicinal plants used to treat endoparasites and stomach problems in dogs, cats and pigs in British Columbia, and Canada [107].

It appeared that Agropyron repens was phytotoxic. Favonoids were the compounds which produced the phytotoxic effects [108-109].

3.7 Contraindication and adverse effects:
Couch grass is listed by the Council of Europe as a natural source of food flavoring (category N2). In the United States, it is listed as GRAS (Generally Recognized as Safe). The safety and efficacy of couch grass has not been systematically studied for any indication in available reports. However, traditional use suggests that couch grass is generally well tolerated. Couch grass is accepted in the Indian and Colonial Addendum of the British Pharmacopoeia for use in the Australian, Eastern and North American Colonies, where it is much employed. Excessive and prolonged use of couch grass should be avoided due to its reputed diuretic action, as this may result in hypokalemia (abnormally low potassium levels in the blood). Caution is advised in patients who have edema (swelling) caused by heart or kidney disease. Based on tradition, couch grass should be taken with plenty of fluids to flush out the urinary tract [109-110].

3.8 Dosage:
Dried rhizome 4-8 g or in decoction three times daily. Liquid extract 4-8 ml (1:1 in 25% alcohol) three times daily. Tincture 5-15 ml (1:5 in 40% alcohol) three times daily [84,92,109,111].

The use in children and adolescents under 18 years of age is not recommended. Duration of use: The herbal substance is traditionally used over a period of 2 up to 4 weeks. Method of administration: Oral use [79].

4. Conclusion
This review discusses the chemical constituent, pharmacological and therapeutic importance of Agropyron repens as a promising drug as a result of wide range of pharmacological effects.

References
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Chapter Title

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