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The medical importance of *Cydonia oblonga*- A review

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Abstract: The chemical analysis of *Cydonia oblonga* showed that it contained phenolics, pectin, essential and volatile oils. The analysis of the essential oils of *Cydonia oblonga* leaves showed that the it contained aromatic aldehyde, fatty acid, oxygenated monoterpene, sesquiterpene hydrocarbon and aromatic aldehyde. The quince fruits contained protein, carbohydrate, lipids, and high levels of mineral elements suc as Na, K, Ca, Mg, Fe, Cu, Zn and Mn. This review was designed to highlight the chemical constituents and pharmacological importance of *Cydonia oblonga*.

Keywords: *constituents, pharmacology, medical, Cydonia oblonga*

I. INTRODUCTION

A large and increasing number of patients in the world use medicinal plants and herbs for health purpose. Therefore, scientific scrutiny of their therapeutic potential, biological properties, and safety will be useful in making wise decisions about their use[1-2].

Recent reviews showed that plants produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of many drugs [3-71]

The chemical analysis of *Cydonia oblonga* showed that it contained phenolics, pectin, essential and volatile oils. The analysis of the essential oils of *Cydonia oblonga* leaves showed that the it contained aromatic aldehyde, fatty acid, oxygenated monoterpene, sesquiterpene hydrocarbon and aromatic aldehyde. The quince fruits contained protein, carbohydrate, lipids, and high levels of mineral elements suc as Na, K, Ca, Mg, Fe, Cu, Zn and Mn. This review will highlight the chemical constituents and pharmacological importance of *Cydonia oblonga*.

Plant profile:

Synonyms:

Cydonia cydonia var. *lusitanica* (Mill.) Pers., *Cydonia lusitanica* Mill., *Cydonia vulgaris* var. *lusitanica* (Mill.) DC[71].

Taxonomic classification:

Kingdom: Plantae, **Division**: Magnoliophyta, **Class:** Magnoliopsida, **Order**: Rosales, **Family**: Rosaceae, **Subfamily**: Maloideae, **Genus**: *Cydonia*, **Species**: *Cydonia oblonga*[72].

Common names:

Arabic: Sefarjal; **Chinese**: Wen po; **English**: Quince; **French**: Cognassier, Coing; **German**: Quitte, Quittenbaum; **Portuguese:** Marmelo; **Russian:** Ajva; **Spanish**: Membrillero**; Swedish**: Kvitten[73]**.**

II. DISTRIBUTION

Cydonia is native to western Asia, and the center of origin is considered to be the Trans-Caucasus region including Armenia, Azerbaijan, Iran, southwestern Russia, and Turkmenistan. During ancient times, quince spread from its wild center of origin to the countries bordering the Himalaya Mountains to the east, and throughout Europe to the west[73-74]. Now it is distributed worldwide, Turkey is the largest producer with about 25% of world production. China, Iran, Argentina, and Morocco, each produce less than 10%. The United States is a very minor producer of quince fruit, mainly in California's San Joaquin Valley[75].

Description:

Cydonia oblonga is a monotypic genus. It grows as a multi-stemmed shrub or small tree and has pubescent to tomentose buds, petioles, leaves, and fruit. Leaves are ovate to oblong, about 2 inches (5 centimeters) across and 4 inches (10 centimeters) long. The solitary white flowers are 1½ to 2 inches (4 to 5 centimeters) across, have 5 petals, 20 or more stamens, 5 styles, an inferior ovary with many ovules. Bloom time usually beginning mid April in the central latitudes of the northern hemisphere. The fruit is a fragrant, many-seeded pome about 3 inches (8 centimeters) in diameter. Shape ranges from round to pear-like, flesh is yellow[74].

Traditional uses:

Traditionally, the leaves were used as astringent and antiseptic. Fruits were used as astringent, antiseptic, hepatoprotective, cicatrising, anti-inflammatory; for treatment of diarrhoea, dysentery, hepatic disorders, leucorrhoea, haemoptysis, uterine haemorrhages, and wounds. The seeds of *Cydonia oblonga* were used traditionally as astringent, emollient and for the treatment of diarrhea, dysentery, cough, sore throat, bronchitis, intestinal colic and constipation[76-79].

Part used: The parts of the plant used medicinally were leaves, fruits and seeds[79].

III. CHEMICAL CONSTITUENTS

The main nutritional composition of quince fruits in 100 g fresh weight were: energy: 176 kj , protein; 0.6g, acid: 0.9g, carbohydrate: 9.1g, water; 86.9g, ash: 0.6g and fiber: 1.9g. Mineral element contents in 100 g quince fruits were: Na 9.2 mg, K 189 mg, Ca 66 mg, Mg 10 mg, Fe 1.1 mg, P 25 mg, Cu 0.006 mg, Zn 0.013 mg, and Mn 0.002 mg[80-81].

The vitamin contents in 100 g fresh quince fruit were: retinol: 5.5 µg, carotene 0.03 mg, thiamine: 30 µg, riboflavin: 30 µg, niacin : 0.2 mg and ascorbic acid: 13 mg[81-82].

The analysis of the essential oils of *Cydonia oblonga* leaves showed that the leaves of *Cydonia oblonga* contained aromatic aldehyde [benzaldehyde (12.8%)], followed by fatty acid [hexadecanoic acid (7.2%)], oxygenated monoterpene [linalool (5.7%)], norisoprenoid [(E)-β-Ionone (5.1%)], sesquiterpene hydrocarbon [germacrene D (8.6%)] and aromatic aldehyde [benzaldehyde(4.9%)] which represented the main components. However the percentage of the compounds isolated from the oil of *Cydonia oblonga* leaves in the flowering and fruiting periods respectively were: hexanal 0.4 and 0.2, decane trace and - , dodecane 0.6 and - , limonene trace and - , (*Z*)-3-hexenal , 1.3 and 3, amyl furan (2-Pentyl furan) 0.5 and -, terpinolene trace and -, octanal 2.9 and 0.7, (*Z*)-3-hexenyl acetate - and 1.4, (*Z*)-3-hexenol – and 3.8, nonanal 5 and 0.8, tetradecane – and 0.8, pentadecane 1.1 and - , decanal 1 and - , benzaldehyde 12.8and 4.9, (*E*)-2-nonenal 0.8 and - , linalool 5.7 and 1.3, (*E,Z*)-nonadienal trace and -, hexadecane 2.5 and - , β-caryophyllene – and 0.9 - , undecanal 1.9 and -, β-cyclocitral 1.3 and - , (*Z*)-3-hexenyl tiglate 0.9 and - , (*Z*)-β-farnesene – and 4.8, selina-4,11-diene (=4,11-Eudesmadiene) – and 0.4, heptadecane 2 and - , α-terpineol 2.2 and 2.3, dodecanal 1.8 and - , germacrene - and 8.6, β-selinene – and 0.7, (*E,E*)-α-farnesene 4.6 and 0.7, naphthalene 1.5 and - , δ-cadinene - and 0.4, γ-cadinene - and 0.1, methyl salicylate – and 0.1, octadecane 1.1 and - , tridecanal 3.9 and 0.5, (*E*)-β-damascenone 1.9 and - , geraniol 3.2 and - , (*E*)-geranyl acetone 0.3 and - , α-ionone 0.2 and - , tetradecanal 1 and - , nonadecane 0.2 and - , benzyl isovalerate – and 0.2, (*E*)-β-ionone 5.1 and 0.5 , dodecanol 0.2 and -, caryophyllene oxide – and 1.9, pentadecanal 4.6 and 1 , (*E*)-nerolidol 0.5 and 1.4, octanoic acid trace and -, hexyl benzoate – and 0.4, hexahydrofarnesyl acetone 1.1 and -, (*Z*)-3-hexen-1-yl benzoate 1.7 and 0.6, (*E*)-2-hexen-1-yl benzoate - and 0.6, T-cadinol - and 4.7, α-cadinol - and 1.5, decanoic acid 1.1 and -, tricosane 0.3 and 2.3, 9-geranyl-*p*-cymene - and 1.5, farnesyl acetone 0.1 and - , undecanoic acid 0.1 and - , tetracosane 0.1 and - , pentacosane 1 and - , dodecanoic acid 0.8 and - , caryophylla-2(12),6(13)-dien-5α-ol (=Caryophylladienol II) - and 0.7, tetracosane - and 0.8 , pentacosane - and 2.8 , geranyl linalool 0.7 and - , tridecanoic acid trace and - , phytol 1 and 3.1, benzyl benzoate – and 0.7, tetradecanoic acid 2.2 and - , heptacosane 3.6 and 1.9, benzyl salicylate 0.2 and - , nonacosane 0.7 and 0.2 and hexadecanoic acid 7.2 and 1.7[83].

However Oliveira *et al*., analyzed the *Cydonia oblonga* Miller leaves phenolic compounds of 36 samples of quince leaves from three different geographical origins, nine phenolic compounds were isolated including 3- O-, 4- O- and 5- O-caffeoylquinic acids, 3,5- O-dicaffeoylquinic acid, quercetin-3- O-galactoside, quercetin-3- O-rutinoside, kaempferol-3- O-glycoside, kaempferol-3- O-glucoside, and kaempferol-3- O-rutinoside. 5- O-caffeoylquinic acid, represented the major phenolic compound, followed by quercetin 3- O-rutinoside. Quince leaves are characterized by higher relative contents of kaempferol derivatives than fruits (pulps, peels, and seeds), especially in what concerns kaempferol-3- O-rutinoside (12.5%). *Cydonia oblonga* leaves total phenolic content was very high, varying from 4.9 to 16.5 g/kg dry matter (mean value of 10.3 g/kg dry matter)[84].

Quince seeds presented a phenolic profile composed of 3-O-caffeoylquinic, 4-O-caffeoylquinic, 5-O-caffeoylquinic and 3,5-dicaffeoylquinic acids, lucenin-2, vicenin-2, stellarin-2, isoschaftoside, schaftoside, 6-C-pentosyl-8-C-glucosyl chrysoeriol and 6-C-glucosyl-8-C-pentosyl chrysoeriol. Six identified organic acids constituted the organic acid profile of quince seeds: citric, ascorbic, malic, quinic, shikimic and fumaric acids[85].

Qualitative and quantitative analyses of phenolic compounds were carried out on quince fruit samples from seven different geographical origins in Portugal. For each origin, both pulp and peel were analyzed by reversed-phase HPLC-DAD and HPLC-DAD/MS. The results revealed differences between the phenolic profiles of pulps and peels. The pulps contained mainly caffeoylquinic acids (3-, 4-, and 5-O-caffeoylquinic acids and 3,5-dicaffeoylquinic acid), one quercetin glycoside (in low amount). The peels presented the same caffeoylquinic acids and several flavonol glycosides: quercetin 3-galactoside, kaempferol 3-glucoside, kaempferol 3-rutinoside,

and several unidentified compounds (probably kaempferol glycoside and quercetin and kaempferol glycosides acylated with p-coumaric acid). The highest content of phenolics was found in peels[86].

Hamauzu *et al.,* found that quince fruit extract had considerable amounts of hydroxycinnamic derivatives mainly composed of 3-caffeoylquinic acid, 5-caffeoylquinic acid and polymeric procyanidins[87].

However, Fattouch *et al.,* mentioned that the total phenolic content of quince (*Cydonia oblonga* Miller) fruit aqueous acetone extracts of the pulp and peel parts ranged from 37 to 47 and 105 to 157 mg/100 g of fresh weight, respectively. Chlorogenic acid (5-O-caffeoylquinic acid) was the most abundant phenolic compound in the pulp (37%), whereas rutin (quercetin 3-O-rutinoside) was the main one in the peel (36%)[88].

However, phenolic compounds of quince jams were included: 3-*O*-, 4-*O*- and 5-*O*-caffeoylquinic acids, 3,5-dicaffeoylquinic acid, quercetin 3-galactoside and rutin[89].

Quince leaves contained organic acid profile, composed of six constituents: oxalic, citric, malic, quinic, shikimic and fumaric acids. *Cydonia oblonga* leaves total organic acid content varied from 1.6 to 25.8g/kg dry matter (mean value of 10.5g/kg dry matter). Quinic acid was the major compound (72.2%), followed by citric acid (13.6%). Significant differences were found in malic and quinic acids relative abundances and total organic acid contents according to collection time, which indicated a possible use of these compounds as maturity markers[90].

However, quince fruit (pulp and peel) and quince jam (homemade and industrially manufactured) contained twenty-one free amino acids. The three major free amino acids detected in pulps were aspartic acid, asparagine, and hydroxyproline. While, the three most abundant amino acids in quince peels were glycine, aspartic acid, and asparagine. Similarly, for quince jams the most important free amino acids were aspartic acid, asparagine, and glycine or hydroxyproline[91].

Two ionone glucosides, 9-O-beta-D-glucopyranosides of (6R)-3-oxo-4-hydroxy-7,8-dihydro-alpha-ionol and 3-oxo-5,6-epoxy-beta-ionol were isolated from quince leaves[92].

The pectin yield from *Cydonia oblonga* was on average of 0·53% on fresh weight. The quince pectin had a high galacturonic content (about 78%), and a degree of methoxylation of about 59% corresponding to a medium-high methoxyl pectin[93].

IV. PHARMACOLOGICAL EFFECTS

Immunological and antiallergic effects:

The effects of the combined *Citrus medica* ssp. limonum *efructibus/ Cydonia oblonga efructibus* (*Citrus medica* ssp limonum and *Cydonia oblonga*: each 0.01 g/ml), and separate products of citrus (0.01 g/ml) and cydonia (0.01 g/ml) were investigated on the immunological pathways involved in seasonal allergic rhinitis (SAR). Peripheral blood mononuclear cells (PBMCs) from five healthy and five grass pollen allergic donors were isolated and analyzed *in vitro* after polyclonal and allergen-specific stimulation of T cells in the presence of the three extracts. The analyses demonstrated acceptable cell survival with no signs of toxicity. Citrus mainly had a selective effect on reducing allergen-specific chronic inflammatory (TNF-α; Citrus compared to Cydonia and Citrus/Cydonia: -87.4 ($p<0.001$) and -68.0 ($p<0.05$), respectively) and Th2 pathway activity (IL-5; Citrus compared to cydonia: -217.8 ($p<0.01$); while, both cydonia and citrus/cydonia mainly affected the induction of the allergen-specific Th1 pathway (IFN-γ; Cydonia and citrus/cydonia compared to citrus: 3.8 ($p< 0.01$) and 3.0 ($p<0.01$), respectively). Citrus and cydonia demonstrated different working mechanisms in the treatment of SAR and the combination product did not demonstrate larger effects than the separate preparations[94].

The immunomodulatory and antiallergic properties of preparations from lemon, *Citrus medica*, and *Cydonia oblonga*, which were used in pharmaceutical products to treat patients suffering from allergic disorders, were investigated. Preparations were analyzed with respect to their impact on the degranulation capacity from basophilic cells as well as mediator release from activated human mast cells *in vitro*, including IL-8 and TNF- α secretion. The results showed that the degranulation of basophilic cells was diminished only in the presence of Citrus, and this effect was compared to the synthetic drug azelastine. Furthermore, Citrus and Cydonia both inhibited the production of IL-8 and TNF- α from human mast cells, and at low concentrations additive effects were observed[95].

The effect of a crude hot-water extract (HW) of *Cydonia oblonga* fruit was studied in type I allergy *in vivo* and *in vitro*. The oral administration of the quince HW-added diet to NC/Nga mice for 63 day showed a significant decrease in the development of atopic dermatitis-like skin lesions under conventional conditions. The concentration of IgE in the serum collected from mice fed with quince HW was also lowered in a dose-dependent manner. Moreover, quince HW inhibited the release of beta-hexosaminidase from rat basophilic leukemia cell line RBL-2H3 after a 24-hr treatment. The quince HW fraction of less than 3 kDa reduced the mRNA expression of the high-affinity IgE receptor (FcepsilonRI) gamma subunit[96].

To compare the efficacy and safety of two routes of administration (nasal spray versus subcutaneous injections) of Citrus/Cydonia in seasonal allergic rhinitis, a randomised, comparative clinical trial with two parallel groups was carried out. After a one- or two-week wash-out period, 23 patients were randomized, to a 6-week treatment

period and the immunological and symptom severity changes and safety were evaluated. Both routes of administration were safe, they demonstrate immunological and clinical effects, with larger inflammatory and innate immunological effects of the nasal spray route and larger allergen-specific clinical effects of the subcutaneous route[97].

In a three-way-crossover study in 18 healthy male and female subjects aged from 20 to 49 years the influence of a 1% and 3% solution of a standardized composition of *Citrus limon*, succus, and extract from *Cydonia oblonga*, fructus (Gencydo) on the intranasal mucociliar clearance was investigated after multiple administration. Neither after intranasal administration of the 1% and 3% Citrus/Cydonia solution nor after placebo solution, a prolongation of the perception time was found. It could be concluded that there was no measurable influence of the test products on the intranasal ciliar function[98].

The effect of a crude hot-water extract (HW) of quince (*Cydonia oblonga* Miller) fruit on immunoglobulin E (IgE)-dependent late-phase immune reactions of mast cells was evaluated using *in vitro* system. Mast cell-like RBL-2H3 cells were treated with quince HW and late-phase reaction was then induced by stimulation with IgE + Antigen. Quince HW reduced the elevation of interleukin-13 and tumor necrosis factor-α expression level. Furthermore, quince HW suppressed these cytokine expressions of mouse bone marrow-derived mast cells (BMMCs). Leukotriene C_4 and prostaglandin D_2 production in BMMCs were also reduced by treating the cells with quince HW after 1 and 6 h of stimulation. The induction of intracellular cyclooxygenase (COX)-2 expression but not COX-1 expression in BMMCs was also reduced by quince HW[99].

V. ANTIOXIDANT EFFECTS

In comparison of antioxidant potential of quince leaf and green tea (*Camellia sinensis*). Quince leaf exhibited a significantly higher reducing power than green tea (227.8 ± 34.9 and 112.5 ± 1.5 g/kg dry leaf, respectively), but showed similar 2,2'-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging activities. Quince leaf methanolic extract significantly protected the erythrocyte membrane from hemolysis under the oxidative action of 2,2'-azobis(2-amidinopropane) dihydrochloride[100].

The radical scavenging potential of the extracts was determined and compared with that of synthetic antioxidants. The stronger properties corresponded to those obtained from peel material with a 70-80% inhibitory effect on DPPH radicals[88].

The antioxidant functions of quince phenolic extracts were superior to that of chlorogenic acid and ascorbic acid, evaluated in both the linoleic acid peroxidation system and the DPPH radical scavenging system[87].

The antioxidant activity of quince fruit (pulp, peel, and seed) and jam, methanolic extracts were fractionated into a phenolic fraction and an organic acid fraction and were analyzed by high-performance liquid chromatography/diode array detection and HPLC/UV. Antiradical activities of the extracts and fractions were evaluated by a microassay using 1,1'-diphenyl-2-picrylhydrazyl. The phenolic fraction exhibited a stronger antioxidant activity than the whole methanolic extract. Organic acid extracts were the weakest in terms of antiradical activity, which indicated that the phenolic fraction gave a higher contribution for the antioxidant potential of quince fruit and jam. The evaluation of the antioxidant activity of methanolic extracts showed that peel extract exerted the highest antioxidant capacity. The IC_{50} values of quince pulp, peel, and jam extracts were correlated with the caffeoylquinic acids content. Among the phenolic fractions, the seed extract was the one that exhibited the strongest antioxidant activity[101].

Cydonia oblonga fruit were separated into pulps, peels and seeds and methanolic extracts of these parts were prepared. Antioxidant properties were studied for their ability to quench the stable free radical 2,2'-diphenyl-1-picrylhydrazyl (DPPH) and to inhibit the 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH)-induced oxidative hemolysis of human erythrocytes. Pulp and peel extracts showed similar DPPH free radical scavenging activities (EC_{50} of 0.6 and 0.8 mg/ml, respectively), while seed extract presented much lower antioxidant potential (EC_{50} of 12.2mg/ml). Under the oxidative action of AAPH, pulp and peel extracts showed significant protection of the erythrocyte membrane from hemolysis, in a time- and concentration-dependent manner[102].

The antioxidant potential of *Cydonia oblonga* leaf, compared with green tea, was studied by Folin-Ciocalteu reducing capacity assay and by the ability to quench the stable free radical 2,2'-diphenyl-1-picrylhydrazyl (DPPH) and to inhibit the 2,2'-azobis(2-amidinopropane) dihydrochloride (AAPH)-induced oxidative hemolysis of human erythrocytes. Quince leaf exhibited a significantly higher reducing power than green tea (mean value of 227.8 ±34.9 and 112.5 ± 1.5 g/kg dry leaf, respectively). Quince leaf extracts showed similar DPPH radical-scavenging activities (EC_{50} mean value of 21.6 ± 3.5 microg/ml) but significantly lower than that presented by green tea extract (EC_{50} mean value of 12.7 ± 0.1 microg/ml). Under the oxidative action of AAPH, quince leaf methanolic extract significantly protected the erythrocyte membrane from hemolysis in a similar manner to that found for green tea (IC_{50} mean value of 30.7 ± 6.7 and 24.3 ± 9.6 microg/ml, respectively, $P > 0.05$)[100].

The antioxidant effects of lipophilic quince wax extract (QWE) and an aqueous fermented one (QAFE) were studied including their radical scavenging and reductive power as well as their antilipoperoxidative properties.

The Quince Aqueous fermented extract (QAFE) effectively scavenged the radical target species exhibiting ID_{50} values equal to 68.8 µg/ml towards DPPH· and 73.7 µg/ml towards the anion superoxide radical. Quince wax extract (QWE) was more effective at preventing the formation of thiobarbituric reactive species than QAFE, exhibiting an ID_{50} value equal to 48.9 µg/ml[(103)].

Antimicrobial effect:

The antimicrobial activity of *Cydonia oblonga* leaves extracts against different microorganism strains was also investigated. Quince peel extract was the most active for inhibiting bacteria growth with minimum inhibitory and bactericide concentrations in the range of 102-5 x 10^3 microg polyphenol/ml. It appeared that chlorogenic acid acts in synergism with other components of the extracts to exhibit their total antimicrobial activities[(88)].

The ethanolic extract of *Cydonia oblonga* seeds was dissolved in dimethylsulfoxide (DMSO) to obtain the final concentrations: 500, 250, and125 mg/ml and the agar well diffusion method was used to determine antibacterial activity of extract. Six millimeter diameter wells were punched in to the agar and filled with 0.1ml of each extract. Solvents were used as negative control. Tract exexhibited antibacterial activity against *s. aureus* at all concentrations and the sensitivity increases directly with increasing the concentration, *s. epidermids* was sensitive at 500 mg/ml and *k. pneumonia* was sensitive at 250mg/ml. *E. coli* and *Moraxella* were resistant to ethanolic extract[(104)].

The antibacterial effects of *Cydonia oblonga* fruit and seed (ethanolic, acetonic and aquatic extracts) were studied on some dermatic bacteria such as Pseudomonas aeruginosa, Staphylococcus aureus and Staphylococcus epidermidis. Ethanolic extract of quince seed was the most effective extract. Quince seeds extracts showed more antibacterial effect compared with Quince fruit. The aquatic extracts didn't show antibacterial effect[(105)].

The antibacterial effects of extracts of the fruit and seed of *Cydonia oblonga* Miller was studied against *Klebsiella pneumoniae*, *Escherichia coli* and *Enterobacter aerogenes*. The results showed that the ethanolic extract of seeds was the most effective. *E. coli* was the most sensitive bacterium to the extracts, and aqueous extract only showed antimicrobial effect against *E. aerogenes*[(106)].

The antimicrobial activity of *Cydonia oblonga* was studied *Cydonia oblonga* was performed by the diffusion method in dishes with disks embedded at the concentrations of 100, 200 and 400 mg/ml fruit decoction and crude extract from *Cydonia oblonga* leaves, were tested against six bacteria. The crude extract from leaves showed antibacterial activity, it partially inhibited the growth of *Streptococcus agalactiae*[(107)].

The antimicrobial effect of extracts from quince fruits was investigated against foodborne pathogenic (Staphylococcus aureus) strains. The antimicrobial effect was investigated by rapid impedance method. The antimicrobial effect of extracts was confirmed by decreasing of the integrated area of the impedimetric growth curve[(108)].

The *in vitro* anti-Helicobacter pylori activity of 33 substances, juices and plant extracts and 35 of their combinations were tested using an agar diffusion method on Columbia blood agar. Quince (*Cydonia oblonga*) juice demonstrated the strongest anti-H. pylori activity followed by cranberry juice[(109)].

The antifungal effects of ethanolic and acetonic extracts of *Cydonia oblonga* leaves were studied against Aspergillus niger. The results showed that the *Cydonia oblonga* extracts inhibited the growth of A. niger and ethanolic extract was more effective than acetonic extracts[(110)].

Anti-influenza viral activities of quince fruits phenolic extract was studied. Quince phenolics showed anti-influenza viral activity on the hemagglutination inhibition test[(87)].

VI. CARDIOVASCULAR EFFECTS

The effect of ethanol leaf extracts of *Cydonia oblonga* Mill. (COM) was studied on hypertension and on biomarkers associated with blood pressure control, such as angiotensin-II (AII), plasma renin activity (PRA), apelin-12 (A), endothelin (ET) and nitric oxide (NO), compared to captopril. Two-kidney one-clip (2K1C) Goldblatt model rats were divided randomly into six groups: sham, model, captopril 25 mg/kg, COM leaf extract 80, 160 and 320 mg/kg. Drugs were administered orally daily for eight weeks. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured before treatment and every 2 weeks. Blood and kidney samples were collected after the last treatment to measure AII, PRA, A, ET and NO. Renal hypertensive rats (RHR) had increased blood pressure, AII, A, PRA, ET and decreased NO. Treatment with captopril reduced blood pressure, AII, A, PRA, and ET, though not quite to normal values. COM leaf extracts significantly and dose-dependently reduced blood pressure, AII, A, RA and ET, whereas NO was increased. The effects of COM extracts on blood pressure and biomarkers were dose-dependent and at the highest dose, it produced effects similar to those of captopril[(111)].

The effects of *Cydonia oblonga*. (COM) fruit and leaf extracts on blood pressure and rheology were studied in renal hypertensive rats (RHR). Daily doses of 80 and 160mg/kg aqueous or ethanol extracts of COM fruit or leaves, or 25mg/kg captopril were given orally once daily for 8 weeks. Blood pressure was measured before treatment and every 2 weeks thereafter. Blood rheology was tested after 8 weeks. Model rats had higher blood

pressure than sham, 8 weeks after the procedure (systolic blood pressure 193±7 vs. 138±8mmHg, $p<0.05$). Those treated with captopril had decreased blood pressure within 2 weeks but that did not return to the level found in the sham group at 8 weeks (167±7, $p<0.05$ vs. model). With the COM extracts, the effect on blood pressure was notable after 4 weeks. At 8 weeks blood pressure was similar with captopril and with 160mg ethanol leaf extract (166±4, $p<0.05$ vs. model), it was the most effective of the extracts. Model rats had higher blood viscosity and lower erythrocyte deformability than sham. Captopril had little effect on blood rheology; whereas COM extracts reduced whole blood viscosity and improved erythrocyte deformability to levels approaching those found in sham[112].

The hypolipidemic effect of *Cydonia oblonga* was studied in a rat model. low-, medium- and high-dose *Cydonia oblonga* leaf extracts (COM) were given orally for 56 days. The normal controls were fed a normal diet, all other groups a high fat diet. COM dose-dependently reduced TC, TG, LDL-C and MDA, inhibited the activity of ALT, AST and LPS, increased HDL-C content, increased the activity of SOD, GSH-PX, LPL and HL, and reduced liver steatosis in hyperlipidaemia rats, significant at medium and high doses. The effect of COM was similar to that of simvastatin except for increased lipoprotein lipase and hepatic lipase which were reduced by COM but not by simvastatin[113].

The effects of *Cydonia oblonga* Miller (COM) total flavonoids (TF) from leaves and fruit on the blood lipid and antioxidant potentials were studied using hyperlipidaemic rat models. Compared with the hyperlipidaemic model group, TF significantly reduced serum TC, TG, LDL-C ($p<0.01$), ALT and AST ($p<0.01$ or $p<0.05$) and increased HDL-C ($p<0.05$ or $p<0.01$). TF also reduced MDA ($p<0.01$ or $p<0.01$)[114].

The effects of hydromethanolic extract of quince leaf was investigated on the lipid profile of rabbits fed with cholestrol enriched diet (2% w/w for two months). Animals were treated as follow: no treatment (NT), atrovastatin (AT) (0.5 mg/kg/day) and quince extract (QE) (dried extract, 50 mg/kg/day) treatment, and then fed with normal diet for three months. Significant increases ($p<0.05$) in the mean values of cholestrol I, triglyceride, low density lipoprotein, aspartate aminotransferase, alanine transaminase, creatinine, and alkaline phosphatase with a significant decrease ($p<0.05$) in high density lipoprotein level, were recorded after receiving cholestrol enriched diet in comparison with the control group[115].

The effects of *Cydonia oblonga* Miller (COM) extracts was investigated on models and markers of thrombosis and related biomarkers in mice. 20, 40, 80 mg/kg/day COM aqueous extracts or 5mg/kg/day aspirin, were given orally for 14 days and were compared to untreated controls regarding bleeding and clotting times, using the tail cutting and glass slide methods and for death rates in collagen-epinephrine pulmonary thrombosis, thrombolysis *in vitro* and euglobulin lysis time (ELT). Common carotid artery $FeCl_3$-induced thrombus and inferior vena cava thrombosis occlusion time, plasma concentrations of thromboxane B2 (TXB2) and 6-keto-prostaglandine F1α (6-keto-PGF1α) were measured. Compared to controls, COM extracts dose-dependently prolonged bleeding by 2.17, 2.78 and 3.63 times, compared with aspirin 2.58, and the clotting time by 1.44, 2.47 and 2.48 times, compared with aspirin 1.91. COM reduced pulmonary embolus mortality by 27, 40 and 53%, compared with 47% for aspirin. COM dose-dependently increased thrombolysis by 45, 55 and 63%, compared with 56% for aspirin, and shortened ELT to 71, 61 and 43%, compared with 43% for aspirin. In rats, venous occlusion time was prolonged. Arterial and venous thrombus weights were dose-dependently reduced in COM groups. TXB2 decreased and 6-keto-PGF1α increased with COM and aspirin, with an association between 6-keto-PGF1α/TXB2 and arterial or venous thrombus weight for all products, and for occlusion time with COM but not for aspirin[116].

VII. EFFECT ON GIT AND RESPIRATORY SMOOTH MUSCLE CONTRACTION

The pharmacological rationalization for the medicinal use of *Cydonia oblonga* in gut and airways diseases was investigated. Results showed that the crude extract of *Cydonia oblonga* seeds (Co.Cr) produced atropine sensitive spasmodic effects in isolated ileum of guinea-pig and rabbit jejunum preparations. In rabbit jejunum, Co.Cr also showed relaxant activity at slightly higher concentrations (0.1-10 mg/ml). When analyzed on rabbit jejunum pre-contracted with K^+ (80 mM), the plant extract (0.003-10 mg/ml) produced relaxation. A rightward shifting of Ca^{++} dose-response curves along with decline in the maximum response was observed after pretreatment with Co.Cr (0.003-0.01 mg/ml), which was similar to the effect of verapamil. The crude extract of *Cydonia oblonga* seeds (Co.Cr) (0.01-10 mg/ml) relaxed CCh (1 μM) and K^+ (80 mM)-induced contractions of isolated rabbit tracheal preparations, similar to the effect produced by verapamil[117].

The effect of quince juice (QJ) and quince hydroalcoholic extract (QHE) on ulcerative colitis (UC) induced by TNBS (trinitrobenzene sulfonic acid) was studied in rats. Rats were grouped and fasted for 36 hr before colitis induction. TNBS was instilled into the colon with a hydroalcoholic carrier and then treated for 5 days starting 6 h after colitis induction with different doses of QJ (200, 400, 800 mg/kg), QHE (200, 500 & 800 mg/kg) orally, QJ (400 mg/kg) and QHE (200 and 500 mg/kg) intraperitoneally. The colon tissue was removed and tissue damages were scored after macroscopic and histopathologic assessments. The examined doses of QJ and QHE were effective to reduce the extent of UC lesions, only the greatest doses (500 and 800 mg/kg) resulted in

significant alleviation. Weight/length ratio as an illustrative of tissue inflammation and extravasation was also diminished with quince treatments [118].

Cydonia oblonga fruit preparations reduced the gastrointestinal propulsion and inhibited castor oil-induced diarrhoea in mice[119].

VIII. REPRODUCTIVE EFFECT

The effect of quince (*Cydonia oblonga* Miller) leaf decoction was evaluated in testicular injury and impaired spermatogenesis induced by hypercholesterolemia in rabbits. Mature New Zealand white male rabbits were randomly divided into three groups: group 1 (hypercholesterolemia), group 2 (hypercholesterolemia plus quince treatment), and group 3 (control). Groups 1 and 2 received a cholesterol-enriched diet for six weeks. Group 2 received *Cydonia oblonga* leaf decoction as drinking supplement as well. After six weeks, a normal diet was substituted in groups 1 and 2 for another six weeks. Group 3 (control group) was maintained throughout the study on a regular diet. At the end of the 12th week, the left testes of the animals were resected for light microscopic study for evaluation of the maturity of germ cells in seminiferous tubules using Johnsen's score. Increase in intertubular connective tissue and diameter of vessels, abundant spermatogonia and primary spermatocytes along the reduced germinal epithelium were noted in all rabbits of the group 1. The animals in groups 2 and 3 had no significant changes in their testicular sections. The mean Johnsen's score of group 1 (4.20 ± 1.92) was significantly lower than that of group 2 (7.33 ± 0.52) and group 3 (7.05 ± 0.07). ($p=0.01$). According to the results , authors concluded that quince leaf decoction (*Cydonia oblonga*) protected rabbit testes and spermatogenesis from damage induced by hypercholesterolemia[120].

The aphrodisiac activity of the hydroalcoholic extract of the fruits of *Cydonia oblonga* was studied in Wistar rats. The extract was administered orally by gavage in the dose of 500 and 800 mg/kg bw per day as a single dose for 28 days. The results showed that after administration of the extract, mounting frequency and the mating performance of the rats increased highly significantly ($p<0.01$). The extract also influenced the behaviour of treated animals in comparison to non-treated rats in a remarkable manner, making them more attracted to females[121].

Dermatological effect:

The healing effect of quince seed mucilage on the skin lesions induced by T-2 toxin was studied in rabbits. Rabbits received 5, 10, and 15% mucilage treatment. A solution of T-2 toxin (83 mg/ml) in methanol was prepared and 12 µl were applied on skin twice with 24 h interval. On the day eight, erythema and inflammation with grown hairs were observed. The complete healing of the skin damage was recorded in rabbits treated by 10 and 15% guince seed mucilage. The proposed mechanisms of healing effects of quince seed mucilage were: preventing impaired protein synthesis by T-2 toxin, acting as an obstacle between T-2 toxin and skin along with reducing water evaporation and acting as antioxidant[122].

Anticancer effect:

Moreover the cytotoxic effects of lipophilic quince wax extract (QWE) and an aqueous fermented one (QAFE) against human HepG2, A549, and HeLa cell lines were evaluated. The two preparations exerted a different effect on the proliferation of the three tested cell lines. Noteworthy, QAFE was almost always more active than QWE but, sometimes, its effects seemed to be strongly dependent on exposure time[103].

The antiproliferative properties of quince (*Cydonia oblonga* Miller) leaf and fruit (pulp, peel, and seed) was investigated against human kidney and colon cancer cells. Quince leaf and fruit extracts exhibited distinctive antiproliferative activities. The extracts from quince leaf showed concentration-dependent growth inhibitory activity toward human colon cancer cells (IC_{50} = 239.7 ±43.2 microg/ml), while no effect was observed in renal adenocarcinoma cells. The seed extracts exhibited no effect on colon cancer cell growth, whereas a strong antiproliferative efficiency against renal cancer cells was observed for the highest concentration assayed (500 microg/ml)[123].

Antiinflammatory effect:

The anti-inflammatory effect of polyphenolic extract from the Tunisian quince *Cydonia oblonga* Miller was investigated. Lipopolysaccharide (LPS) treatment of human THP-1-derived macrophages stimulated secretion of the pro-inflammatory cytokine TNF-α and the chemokine IL-8. Quince peel polyphenolic extract inhibited these changes in a dose-dependent manner. Concomitantly, quince polyphenols enhanced the level of the anti-inflammatory cytokine IL-10 as well as IL-6 secreted by LPS-treated macrophages. The increase in IL-6 secretion that occurred when quince polyphenols were associated with LPS treatment was partially responsible for the polyphenols-mediated inhibition of TNF-α secretion. Biochemical analysis showed that quince polyphenols extract inhibited the LPS-mediated activation of three major cellular pro-inflammatory effectors, nuclear factor-kappa B (NF-κB), p38MAPK and Akt[124].

Antidiabetic effect:

The antidiabetic activity of quince leaves hydro-ethanolic extract was studied in normal and streptozocin-induced diabetic rats. There was no significant effect on normal rats glucose, while, a significant reduction in the blood glucose levels was recorded in diabetic rats at a time period of 0 to 3 h[(125)].

Protective effects:

The putative role of quince (*Cydonia oblonga*) leaf extract in protection and/or alleviation of the negative impacts of UVA on some biochemical and hematological variables was studied in economically important African catfish. A significant ($P<0.05$) decrease in the red blood cell counts, hemoglobin and hematocrit were recorded in the groups exposed to UVA compared to the control groups. Exposure to UVA induced marked red cell shrinkage (increased mean cell hemoglobin concentration) and showed an elevation in mean cell volume and mean cell hemoglobin in the blood of the exposed fish compared to the control. A significant ($P<0.05$) reduction in the total white blood cells was also recorded in the exposed fish compared to the control. The biochemical parameters (blood glucose, total plasma protein, blood cholesterol, plasma creatinine, aspartic amino transferase and alanine amino transferase) were also exhibited a significant increase in the blood of fish exposed to UVA. Methanolic extract of quince leaf before ripening of the fruits had the ability to prevent hematotoxic stress induced by UVA and resulted in enhancement of the immune system of catfish represented by significant ($P<0.05$) increase in the number of white blood cells and lymphocytes of the catfish. Quince extract also protected the red blood cells and biochemical parameters from UVA effects[(126)].

The efficacy of quince extracts (*Cydonia oblonga*) against hyperlipidemia-induced renal injury was studied in rabbits fed on a cholesterol-rich diet with and without a quince leaf extract supplement. Mild glomerular injury and moderate tubular damage were apparent in all rabbits in diseased untreated group, while only milder tubular injury was detected in all animals in groups treated by quince extracts[(127)].

Side effects:

Health risks or side effects following the proper administration of designated therapeutic dosages were not recorded. Because quince mucilage was prepared from the whole seeds, and/or the whole seeds are taken internally, the cyanogenic glycosides are credited with a slight toxicological relevance[(128)].

Dose:

It was used as a powder, a lotion, a decoction and an extract. Preparation: Extract/ decoction: 1 tsp. -of whole seeds per cup of water. A viscous poultice was prepared from the ground seeds[(128)].

IX. CONCLUSION

This review discuss the chemical constituent, pharmacological and therapeutic effects of *Cydonia oblonga* as promising herbal drug because of its safety and effectiveness.

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