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Traditional uses and pharmacological properties of *Alhagi maurorum*: A review

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ABSTRACT

Desert plants contain important phytochemicals which are cheap source of medicine for local communities. These phytochemicals are much better than synthetic medicine due to their harmless effect. *Alhagi maurorum*, belonging to family Leguminosae, is an highly branched spiny shrub which reaches up to 1.5 to 4 feets in height. Roots may reach up to the depth of 15 meters. *Alhagi maurorum* is used in folk medicine, as a purgative, diaphoretic, expectorant and diuretic used to treat piles, migraine, warts and rheumatism. The reviewed information suggests that the plant has got enormous scope for phytochemical and pharmacological studies to substantiate its therapeutic potential.

1. Introduction

Natural products have interesting and useful biological activities and they also perform various functions[1]. Researchers are increasingly turning their attention toward natural products in order to develop better drugs against cancer, as well as viral and microbial infections[2]. There are more than 35 000 plant species which are used in different human cultures around the world for medicinal purpose. According to both recent and previous investigators, phenols, polyphenols and flavonoids are natural antioxidant products of plants and they are present in different concentrations mostly in medicinal plants[3-6].

The family Leguminosae is comprised of about 550 genera and more than 13 000 species which are used in folklore medicine[7]. The family provides us with many edible plants as well as a variety of medicinal plants that constitute an important source of raw materials used in the pharmaceutical industries. In subfamily Fabaceae, several species have been explored. Their flowers are solitary or in pairs in axils and along twigs, with deep red to purple papilionate petals. Leaves are small, deciduous, simple, present at base of each side twig, obovate to oblong, shortly petiolate, with rounded tip, up to 2 cm. The intricately branched spiny shrub reaches 1.5 to 4 feets in height. *Alhagi maurorum* (*A. maurorum*) is the single species of genus *Alhagi* (Fabaceae) found in Iraq, locally known as Aqual[8]. *Alhagi* species have proportionally the deepest root system of any plants. A 1 m high shrub (Figure 1) may have a main root more than 15 m long due to their deep root system *Alhagi* species are drought-avoiding plants that utilize ground water, adapting in that way perfectly to the hyper-arid environment[9].

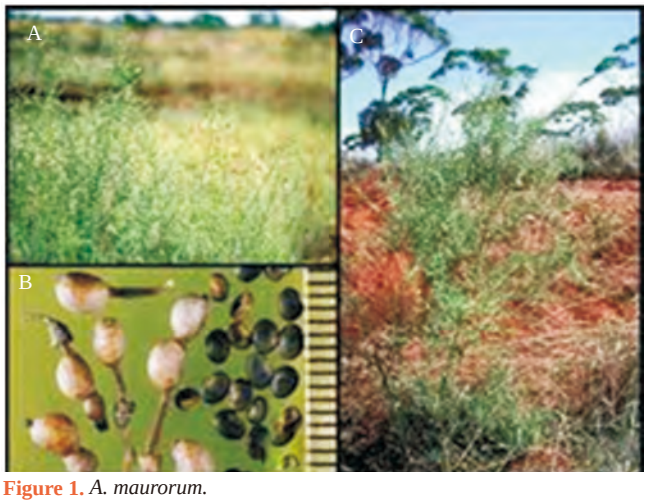

Figure 1. *A. maurorum.*
A, C: Plant body; B: Seeds.

In local communities, this plant is found to be beneficial against rheumatoid, liver disorders, infections of urinary tract, and stomach

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and intestinal disorders. Every part of plant can be drunk for the treatment of hemorrhoids[10].

The alcoholic extract of *A. maurorum* exhibits anti-diarrheal activity *in vivo* at the oral dose of 200 and 400 mg/kg. One of the possible mechanisms of action was due to calcium channel blocking effect[11]. In folk medicine, *A. maurorum* is considered to be effective for the cure of different aliments like bilharzias, rheumatism, liver diseases, urinary and digestive disorders[12]. Its flowers and leaves oil are used for treatment of piles, migraine, warts and rheumatism. Water extracts of its roots are used to enlarge the ureter and to remove kidney stones locally[13-15].

A. maurorum is basically an Arabic name and its vernacular name is Al-Agool, Shouk Aljemal, Hai, Agool, Shabram, Al lahlah, Shouk, Aljam and common name is Camelthorne. It is commonly called as Akool, Camel thorn, Persian Manna plant in Iraq, Saudia Arabia and Persia, respectively[10].

2. Geographical distribution

The plant is found in temperate and tropical Eurasia and the Middle East, Northern India, Afghanistan, Armenia, Azerbaijan, Northwest China, Cyprus, Iran, Iraq, Israel, Jordan, Kazakhstan, Kuwait, Lebanon, Mongolia, Pakistan, Syria, Tajikistan, Turkey, Turkmenistan, Uzbekistan and Russia. In China, the plant is mainly distributed in Xin Jiang Uighur Autonomous Region. In India, it is mostly found in arid and dry regions of Gujarat, Punjab, Uttar Pradesh and Rajasthan[16].

3. Ethnobotanical uses

A. maurorum is used in folk medicine, as a purgative, diaphoretic, expectorant and diuretic[17]. Its flowers are used to treat piles, migraine, and warts. Oil from the leaves is used in the treatment of rheumatism[18]. Locally, water extracts of its roots are used to relax the ureter and to remove kidney stones and it contains alkaloids[17].

Ethnomedicinally, the plant *A. maurorum* is used for diverse topical infections in the different culture of Khyber Pakhtunkhwa Pakistan. In Iran, the decoction of this plant is used for treatment of jaundice, appetite suppressant, diuretic, febrifuge[19].

Different diseases like rheumatism, bilharzias, gastric disorders and infections of urinary bladder are believed to be cured by camel thorn in folk medicine. It has both peripheral and central anti-nociceptive activity on the dose of 400 mg/kg which works as antioxidant[20]. Recently, these plants are proved to have anti-diarrheal activity and induce relaxation of the smooth muscle and antinociceptive effect[18,21,22].

Traditionally, this plant is used for gastrointestinal disorders, gastric ulcer and rheumatism. An aqueous extract of the whole plant of *A. maurorum* is used in traditional medicine in southwest of Iran to treat heartburn resulted from gastric reflux. Phytochemical studies on this plant have revealed the presence of unsaturated sterols, triterpenes, tannins, carbohydrates, flavonoids[11].

4. Impact of *Alhagi (A. maurorum)* in veterinary medicine and animal nutrition

A. maurorum is a medicinal plant used in ethno-veterinary for the treatment and cure of gastrointestinal diseases in domestic animals (cattle, sheep, goats and camels)[23]. It has been reported that the distilled product of *A. maurorum* in goat can control the pH of urine within the normal range. In overall, distilled product of *Alhagi* can be used as a diuretic drug at dose of 8.16 mL/kg in the goats[24]. The effects of supplemented *A. maurorum* meal to broiler chicken was investigated and found that supplementation for 2% of total mixed diet didn't have negative effect on immunological and biochemical measures of serum and also has significant positive effect on performance[25].

5. Medicinal aspects listed in Holy Quran

The plant is mentioned in the Quran as a source of sweet manna[26]. Ancient and religious literatures include natural medicinal notes that are useful for mankind. In this regard, Holy Quran is a unique literature for social and life science research. The Quran had recommended medicinal plants for treatment of various diseases and food[27-30].

Quranic name of *Alhagi* is Alman and was mentioned in different chapters (surah), for example, Bakara (verse 57): "we send you *Alhagi* and quail for beneficial use as food, but they had thankless to these gifts, in fact they had oppression to themselves"; Araf (verse 160): "we divided Bani-Israel into twelve tribes and we had order for Musa that give your cane, next twelve springs were running, we send you *Alhagi* and quail as gifts, and order for eating pure gifts, but they had oppression to these gifts and themselves"; Taha (verses. 80–81): "height Bani-Israel, we rescue you from enemies and put your resort in Toor Mountain, and send for you, *Alhagi* and quail as gifts"[31].

6. Phytochemistry

Chemical investigation of the *Alhagi* species revealed the presence of several contents such as fatty acids and sterols[32], coumarins, alkaloids and vitamins[33]. Twelve flavonoids were isolated from *Alhagi graecorum* Boiss. These flavonoids were identified as tamarixtin 3-*O*-dirhamnoside, isorhamnetin 3-*O*-glucosylneo-hesperidoside, isorhamnetine 3-*O*-robinoside, isorhamnetin 3-*O*-rotinoside, quercetin 3-*O* rhamnoside, kaempferol 3-*O*-galactoside, quercetin 3, 7-diglycoside, isorhamnetin 3-rutinoside, daidzein 7,4-dihydroxyisoflavone, calycisin 3-hydroxyformononetin, and isorhamnetin and tamarxtinaglycones[34]. Phytochemical screening of *A. maurorum* extract revealed the presence of flavonoids, glycosides, alkaloids, saponins, tannins, steroids, and anthraquinone[35,36].

Pharmacological researches on the root extracts of this plant exhibited the activity of these extracts; therefore, extensive efforts were made to know that compound is the active one. Finally, the aliphatic ester glyceryl-*n*-tetracosan-17-ol-1-oate was found to be the active one[23]. Chemical and phytochemical investigation of the ethanol extract of the roots of *A. maurorum* led to the isolation of a new aliphatic ester, which was named glyceryl-*n*-tetracosan-17-ol-1-oate on the basis of spectral data analysis and chemical reactions. This compound, in pure form, was found to enlarge the ureter[37].

Phytochemical screening of crude extracts and its subsequent fractions demonstrated the presence of fats, alkaloids, flavonoids, anthraquinones, cardiac glycosides, coumarins, saponins, phlobatannins, tannins and terpenoids in leaves and roots while the flowers were found to be devoid of any such phytochemical[38]. Phytochemical studies on this plant have revealed the presence of unsaturated sterols, triterpenes, tannins, carbohydrates, flavonoids[11]. Six flavonoids of flavonol type have been isolated from the butanol

fraction of the air dried herb of *A. maurorum*. These compounds were identified as kaempferol, querectin, quercetin 3-*O*-α-rhamnoside, kaempferol-3-*O*-β-glucoside, querectin 3-*O*-β-glucoside and isorhamnetine 3-*O*-β-rutinoside. Phytochemical studies on this plant have revealed the presence of unsaturated sterols, triterpenes, tannins, carbohydrates, flavonoids and flavanone glycosides such as alhagitin and alhagidin and proanthocyanidins[34]. Two flavonoids quercetin and catechin have been isolated from *A. maurorum* with antioxidant activity which inhibit the lipid peroxidation and could counteract with free radicals[39].

Six main flavonoid glycosides were isolated, for the first time, from the ethanol extract of *A. maurorum* Boiss (Leguminosae). They were identified as kaempferol, chrysoeriol, isorhamnetin, chrysoeriol-7-*O*-xylosoid, kaempferol-3-galactorhamnoside and isorhamnetin 3-*O*-b-D-apio-furanosyl (1-2) b-D-galactopyranoside. Their identities were established by m.p., UV, EI-mass, Fab-mass, 600 MHz ^{1}H and ^{13}C NMR. The total extract (300 and 400 mg/kg) and two of the isolated compounds (chrysoeriol-7-*O*-xylosoid and kaempferol-3-galactorhamnoside, 100 mg/kg each) showed a very promising antiulcerogenic activity with curative ratios 66.31%, 69.57%, 75.49% and 77.93%, respectively[40].

Total phenolic and flavonoids contents of camel thorn revealed the higher concentration of flavonoids and phenolic, especially in the ethanol extract. *A. maurorum* is a very common woody perennial shrub, rich in phenolic and flavonoid compounds with more than twelve different isolated flavonoids have been reported[41].

The phytochemicals detected in its various extracts/fractions are well known for various pharmacological activities (Table 1). For example, alkaloids are common antibacterial, antimalarial, cytotoxic and anticancerous agents[42]. Saponins have the insecticidal, antibiotic, fungicidal properties. Anthraquinones are antibacterial, antifungal and cytotoxic agents, while terpenoids are antimalarial and antibacterial agents[43]. Flavonoids have been shown to have antibacterial, anti-inflammatory, anti-allergic, antineoplastic, antiviral, antithrombotic, antioxidant and vasodilatory activities. Tannins have shown potential antiviral and antibacterial effects[44].

Table 1

Important chemical metabolites isolated from *A. maurorum*.

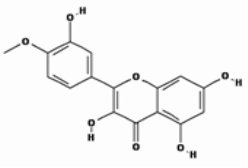
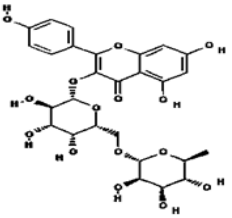
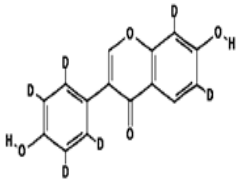
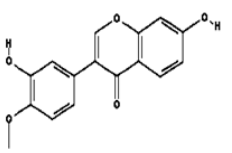
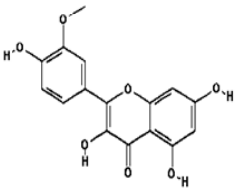
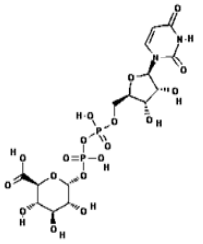
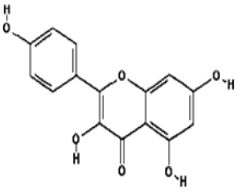
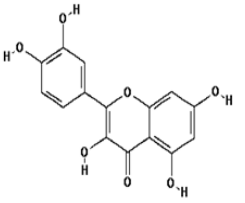
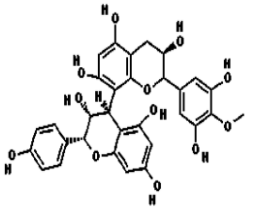
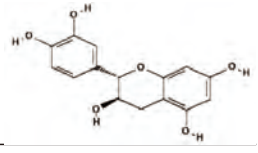
Chemical metabolites	Molecular formula	Chemical structure
Tamarixtin	$C_{16}H_{12}O_7$	
Kaempferol 3-O-galactoside	$C_{27}H_{30}O_{15}$	
Daidzein 7,4-dihydroxyisoflavone	$C_{15}H_{10}O_4$	

Table 1 (*continued*)

Chemical metabolites	Molecular formula	Molecular formula
Calycisin 3-hydroxyformononetin	$C_{16}H_{12}O_5$	
Isorhamnetin	$C_{16}H_{12}O_7$	
Tamarxtinaglycones	$C_{15}H_{22}N_2O_{18}P_2$	
Kaempferol	$C_{15}H_{10}O_6$	
Querectin	$C_{15}H_{10}O_7$	
Proanthocyanidins	$C_{31}H_{28}O_{12}$	
Catechin	$C_{15}H_{14}O_6$	

Phenolic compounds have different biological properties, including antioxidative activities, but they may also be pro-oxidants. The effect of phenolic fraction from roots of *A. maurorum* on oxidative protein/lipid damages in human blood platelets and human plasma after treatment with H_2O_2 was studied *in vitro*. Exposure of blood platelets or plasma to H_2O_2 resulted in a decrease of the level of thiol groups in proteins and an increase of thiobarbituric acid reactive substance. In the presence of phenolic fraction from *A. maurorum* (0.5–50 μg/mL), a reduction of thiol groups oxidation together with the decrease of autoperoxidation of lipids and lipid peroxidation caused by H_2O_2 or thrombin was observed. The phenolic fraction from *A. maurorum*

acts as an antioxidant and can be useful as the natural factor protecting against diseases associated with oxidative stress[45].

Methanol extracts of *A. maurorum* from the aerial part were screened for total phenolic and flavonoids contents, antioxidant, antimicrobial and cytotoxic activities. The antioxidant properties and total phenolic contents of the leaves were higher than those of the flowers. Antimicrobial activities were characterized by inhibition zones and minimum inhibition concentration ranged between 58.0–80.7 and 60.4–84.0 μg/mL, respectively. Leaves and flowers extract induced inhibitory effect against the proliferation of human promyelocytic leukemia cells (HL-60) and IC_{50} was 16.0 and 22.0 μg/mL, respectively. The antimicrobial and cytotoxicity of extracts seemed to be positively correlated with their antioxidant potentials. Leaves and flowers extracts are highly cytotoxic to HL-60 cells and leaves extract was more potent in this regard. *A. maurorum* can be used as possible natural antioxidant, antimicrobial and an effective therapeutic agent in the management of acute promyelocytic leukemia[8].

7. Pharmacology

The ethanol extract of *A. maurorum* powdered roots was examined for its pharmacological activity and showed that administration of ethanol extract intraperitoneally into mice decreased the body temperature in a dose-dependent manner. The decreases ranged from 0.2 to 3.3 ˚C. Treatment of the frog tissue with ethanol extract blocked the action of the neurotransmitter and acetyl choline. Thus, ethanol extract seemed to act as a skeletal muscle relaxant. Intraperitoneal administration of ethanol extract into the anaesthetized rats decreased heart rate by 22.5%, thus, ethanol extract seemed to be a bradycardiogenic drug. The extract induced relaxations to the guinea-pig ureter and suppressed histamine-induced spasms. It seemed to possess a spasmolytic action and a ureter relaxing action that can enhance getting rid of renal stones and relieve of the accompanying pain (contraction of the ureter). The extract did not possess the property of enhancing dissolution of oxalate calculi[22].

The anti-inflammatory, analgesic, antioxidant and antibacterial activities of *A. maurorum* aqueous extract was tested on mice at doses of 125, 250 and 500 μg for each animal. The analgesic and anti-inflammatory potentials were compared with the effect produced by distilled water. It was proved that aqueous extract of this plant possesses significant anti-inflammatory potential but it has no antibacterial potential[10].

The spectrophotometric investigation of the methanol extract found that the leaves and flowers extract had higher phenolic and flavonoid contents and exhibited strong antioxidant activity that was assessed using three different methods. The antioxidant properties and total phenolic contents of the leaves were higher than those of the flowers. Furthermore, a positive correlation has been shown between antioxidant activities assays and total phenolics, indicating that these compounds are more likely to contribute to the antioxidant potential of the investigated plant extracts[9,46,47]. Thus, the phenolic compounds might contribute directly to antioxidative action of plant extract and the antioxidant activity of *A. maurorum* extracts may play an important role in their anti-microbial and anti-proliferative activities[48].

7.1. Antioxidant activity

Antioxidant, anti-diarrheal and anti-ulcerogenic activities of camel thorn has also been reported[33]. Extracts/fractions from leaves of the plant showed strong radicle scavinging activity; it may be due to the presences of phenolic compounds in plant[19]. Leaves and flower extract of camel thorn possesses strong antioxidant potential due to which it shows cytotoxicic effect on the HL-60 cell lines and also possesses antimicrobial activity[8].

7.2. Antifungal activity

The antifungal activities of ethanol extracts of *A. maurorum* Medic. was investigated *in vitro* against *Alternaria alternata*, *Fusarium oxysporum*, *Phoma destructiva*, *Rhizoctonia solani* and *Sclerotium rolfsii* at concentrations of 0%, 3%, 6% and 9% (v/v). Seeds, roots, and rinds had different degrees of antifungal activity against the tested fungi. When compared with the control, the highest antifungal activity was recorded for camel thorn seeds extract at a concentration of 9% and camel thorn rinds extract came in last even when used at a high concentration. The ethanol extract of camel thorn seeds is a potent biofungicide[49].

7.3. Anti-diarrheal activity

The alcoholic total extract of *A. maurorum* exhibits anti-diarrheal activity *in vivo* at the oral dose of 200 and 400 mg/kg. One of the possible mechanisms of action was due to calcium channel blocking effect[22].

7.4. Anti-inflammatory activity

It is proved that the fatal inflammation like histamine and prostaglandin can be cured by this plant due to its inhibitory effect on the release of pro-inflammatory mediators[50].

7.5. Antibacterial activity

The methanolic extract and its derived fractions (*n*-hexane, chloroform, ethyl acetate, *n*-butanol and residual aqueous fraction) of leaves, roots and flowers of *A. maurorum* are subjected as microbicide against *Salmonella typhi*, *Staphylococcus aureus*, *Vibrio cholerae*, *Shigella dysenteriae*, *Escherichia coli* and *Bacillus anthrax*. The antioxidant profile was investigated by 1,1-diphenyl-2-picryl-hydrazyl method and preliminary phytochemical investigations. It was observed that the leaves of the plant showed outstanding response to most bacterial pathogens followed by roots while the fractions from flowers were almost inactive[19].

The ethanol extract of *A. maurorum* showed significant antimicrobial activity against Gram-negative, Gram-positive bacteria as well as unicellular and filamentous fungi[51]. The methanol and hexane extracts of *A. maurorum* showed antimicrobial activities and the methanol extract showed high activity against bacterial strains. Hence, this plant is a potential source of antibacterial drugs[35].

7.6. Antiulcerogenic activity

Gastric damage induced by ethanol was characterized by both long ulcers and petechial lesions. The number of ulcers and the ulcer index in control rats (received ethanol) were highly significant ($P < 0.001$) when compared with normal untreated animals (receiving distilled water). Repeated oral administration of the ethanol extract of *A. maurorum* in doses of 300 and 400 mg/kg reduced the severity of

gastric damage, as the ulcer index was significantly decreased to 2.90 and 2.62 mm, respectively, compared with 8.61 mm in the positive control group. Failure of ranitidine to decrease gastric damage induced by ethanol could be attributed to its mechanism of action, as it blocks the histaminergic receptors, so prevents the stomach from producing excess acid. This mechanism cannot protect the gastric mucosa against the irritant and damaging effects of ethanol. Due to their anti-ulcerogenic activity, they could be used orally either for prophylaxis or for treatment of gastric ulcer[38].

A. maurorum aqueous extract (AME) was tested for anti-ulcer activity in rat. The AME protected rats against water immersion restraint-stress and ethanol-induced ulcers in a dose-dependent manner. In water immersion restraint induced ulcerated rat, the AME increased pH and reduced gastric acid content. AME did not show any signs of toxicity and mortality up to 10 g/kg, *p.o.* in mice. AME has significant mucosal protective and anti-secretory effects on gastric mucosa in rats[52].

7.7. Cytoprotection

A. maurorum has a cytoprotective effect against the gastric mucosa in ethanol-induced gastric lesion in the rats. It is possible that the inhibitory effect of extract is due, at least partly, to the presence of terpenes in *A. maurorum*[11].

7.8. Antidiuretic activity

A. maurorum in a single oral dose of 500 mg/kg significantly ($P < 0.05$) increased urine concentrations of Na^+, K^+ and Cl^-. Repeated oral administration of *A. maurorum* in doses of 500 or 1000 mg/kg significantly ($P < 0.05$) increased urine volume, fractional excretion of sodium and fractional excretion of potassium rate. It is concluded that methanol extracts of *A. maurorum* have a significant diuretic effect[21].

7.9. Antitumour activity

The antitumor activity of *A. maurorum* extracts was studied on the inhibition of cell proliferation in human cancer cell lines *i.e.* lung large cell carcinoma COR-L23, amelanotic melanoma C32, renal cell adenocarcinoma ACHN, breast cancer cell line MCF-7 and hormone dependent prostate carcinoma LNCaP evaluated in comparison with one normal cell line 142BR. Petroleum ether extract showed interesting effect against LNCaP, ACHN, COR-L23, with IC_{50} of 16.68, 10.20 and 14.56 μg/mL, respectively and chloroform extract showed significant activity against LNCaP with IC_{50} 6.25 μg/mL. Kaempferol showed the most significant activity against COR-L23, followed by LNCaP with IC_{50} 10% and 5%, respectively of the IC_{50} of the control drugs. Quercetin showed significant activity against COR-L23 and MCF-7[53].

7.10. Hepatoprotective activity

The administration of 660 mg/kg of the ethanol extract of the *A. maurorum* to mice showed a significant hepatoprotective activity against carbon tetrachloride and acetaminophen, by a significant decrease in the activity of serum transaminases[54]. On the other hand, the cardiac toxicity produced by adriamycine was significantly increased in the presence of the ethanol extract of camel thorn (*A. maurorum*). Camel thorn can protect the liver against the injury produced by carbon tetrachloride or acetaminophen, with unexpected behavior for enhancing the cardiac toxicity of adriamycin in mice[55].

8. Conclusions

A. maurorum is an ethno medicinally important plant and used locally for the treatment of piles, migraine, warts, rheumatism and kidney disorders. Pharmacological studies further confirmed its medicinal importance therefore this plant should be further studied in order to explore its pharmacological potential.

Conflict of interest statement

We declare that we have no conflict of interest.

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