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A review on some endemic and near endemic plants of Toor Al-Baha District, Lahej Governorate, Yemen

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Abstract
The present study aimed at scientifically documenting and evaluating of ten endemic and near endemic plants of the Toor Al Baha district in the Lahej governorate, Yemen. Botanical, ethnobotanical, phytochemical, pharmacological studies of *Aloe sabaea*, *Crinum album*, *Euphorbia fractiflexa*, *Euphorbia fruticosa*, *Euphorbia inarticulata*, *Euphorbia qarad*, *Euphorbia uzmuk*, *Heliotropium longiflorum* var. *longiflorum*, *Pavetta longiflora* subsp. *longiflora* and *Tribulus macropterus* var. *arabicus* have been performed by researching scientific literature and interviewing local people for ethnobotanical uses. 8 out of 10 studied plants were found to be used for humans and animals. The phytochemical constituents were reported for *A. sabaea*, *C. album*, *E. fruticose*, *E. uzmuk* and *Tribulus macropterus* Boiss. var. *arabicus*. Pharmacological studies were reported for *C. album* bulbs, *E. fruticose*, *E. uzmuk*, *Pavetta longiflora* subsp. *longiflora*, and *Tribulus macropterus var. arabicus*. This review provided scientific documentation, encouraged to raise the public awareness against the use of most of the selected plants and highlighted their importance as promising candidates for future scientific research.

Keywords: Botany, chemical constituents, ethnobotanical use, pharmacology, yemeni plants

Introduction
Yemen is very rich in various flora, a portion of which has been used by indigenous people in traditional healing of several diseases [1-5]. Most Yemeni plants have not been scientifically evaluated for their biological activities and safety and hence there is a lack of awareness of the medicinal and toxic properties of these plants. Yemeni flora affords a potential source to be explored not only to understand its healing benefits that could be the basis for new drugs useful in the cure of a number of diseases, but also to understand and avoid its poisonous properties that could represent one of the major risks to livestock and humans. The aim of this study was therefore to scientifically document and evaluate different aspects (botany, chemical constituents, ethnobotanical uses, and pharmacological activity) of ten endemic and near endemic plants growing in Toor Al Baha district, Lahej governorate, Yemen. To the best of our knowledge, this study on the selected plants was performed for the first time and could contribute not only in documenting and preserving indigenous ethnobotanical knowledge but also in providing scientific information for the local authority and health professionals to raise the public awareness about the safety and the rational use of these plants. Furthermore, such a study could form the base for further scientific investigations for phytochemical constituents, pharmacological and toxicological activities of the selected plants.

Materials and Methods
Study area
The plants selected for this study were collected (by the second author) from different habitats of Toor Al-Baha district, Lahej governorate, Yemen during the intensive floristic survey between 2008 and 2017. This study area has a special geographical, bio-geographical and ecological position in the Lahej governorate. It extends between latitudes 12° 58’ and 13° 20’ N. and between longitudes 44° 11’ and 44° 39’ E., with an area of about 1883 sq. km. Toor Al-Baha district is bordered by Al-Qubaytah district in the north, Al-Maqatrah district, Al-Madaribah and Ras Al-Aarah district in the west, Tuban district in the east and by Gulf of Aden and parts of Aden governorate in the south (Fig. 1). Voucher specimens of the collected plants were deposited in the Department of Biology, Faculty of Science, University of Aden.

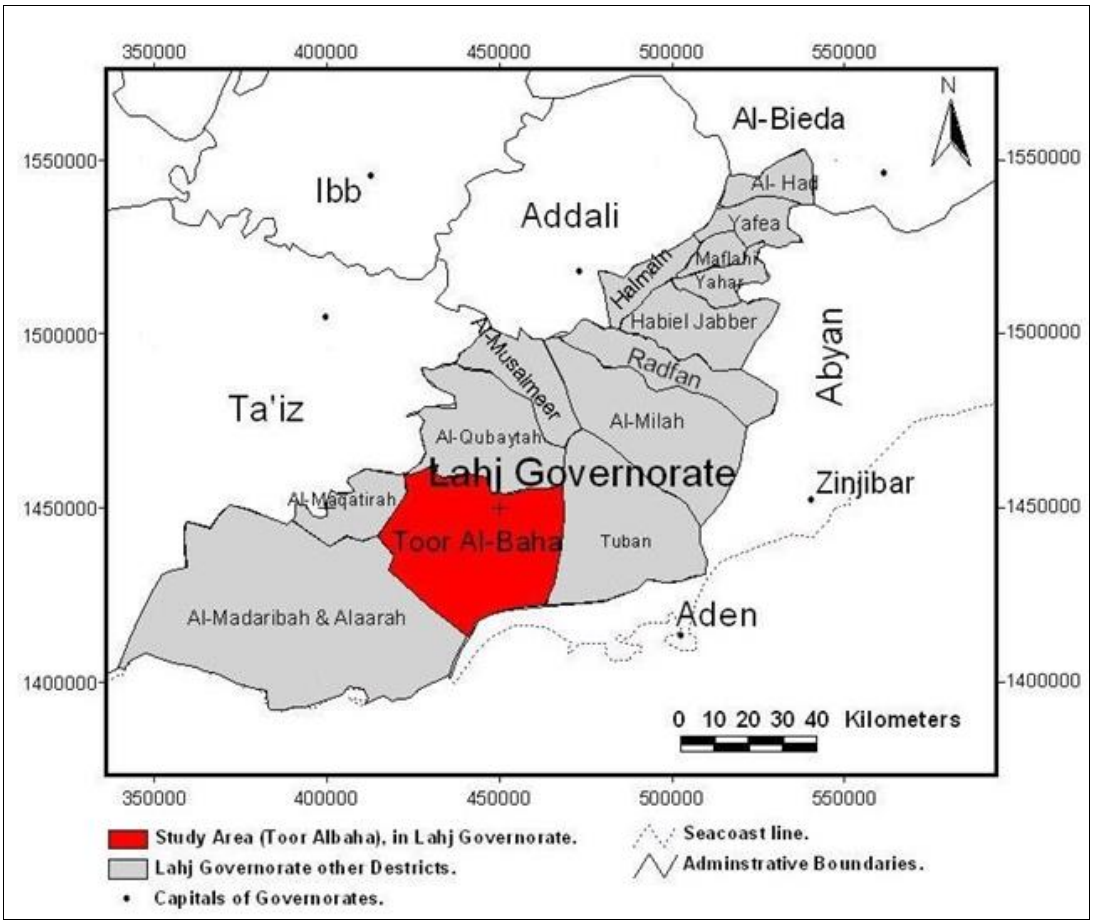

Fig 1: Map of Lahej governorate with browsing the location of study area -Toor Al-Baha district (modified after Ministry of the local administration).

Literature review and data collection

Data on botanical name, family name, synonyms, brief botanical description (with some modifications done by the second author), type, vernacular names, habitat, distribution in Yemen and global distribution of the studied plants were obtained from several references [6-14]. The flowering time was observed by the second author. Furthermore, literature review on chemical constituents, pharmacological activity were obtained by searching different electronic scientific databases via Leiden University library. Ethnobotanical uses were reported by the local people of the study area as well as obtained from electronic databases.

Results and Discussion

Based on field tour in Toor Al-Baha district, ten endemic and near endemic species belonging to 6 genera and 6 families were collected. Three plants are endemic to Yemen, while the other seven plants are near endemic (endemic to Yemen as well as to the Arabian Peninsula) (Table 1).

Table 1: Endemic and near endemic species from Toor Al-Baha district, Lahej governorate, Yemen.

Family	Taxon/Voucher specimen	Endemic	Near endemic
Asphodelaceae	*Aloe sabaea* Schweinf. / Al-Hawshabi (3928)		+
Amaryllidaceae	*Crinum album* (Forssk.) Herb. / Al-Hawshabi (4228)		+
Euphorbiaceae	*Euphorbia fractiflexa* S. Carter & J. R. I. Wood / Al-Hawshabi (1100)		+
	Euphorbia fruticosa Forssk. / Al-Hawshabi (3793)	+	
	Euphorbia inarticulata Schweinf. / Al-Hawshabi (3987)		+
	Euphorbia qarad Defl. / Al-Hawshabi (2757)	+	
	Euphorbia uzmuk S. Carter & J. R. I. Wood / Al-Hawshabi (3660)	+	
Boraginaceae	*Heliotropium longiflorum* (A. DC.) Jaub. & Spach var. *longiflorum* / Al-Hawshabi (1956)		+
Rubiaceae	*Pavetta longiflora* Vahl subsp. *longiflora* / Al-Hawshabi (2734)		+
Zygophyllaceae	*Tribulus macropterus* Boiss. var. *arabicus* (Hosni) Al-Hemaid & J. Thomas / Al-Hawshabi (5018)		+

The collected data on the botany, phytochemical constituents, and pharmacological activity of the selected plants as well as their evaluation are presented as follows:

***Aloe sabaea* Schweinf. (1894), Fig. 2**

Type: Yemen (Schweinfurth, 491, Wadi Madfar, Hodjela).

Synonym: *Aloe gillilandii* Reynolds (1962).

Vernacular names: Adiyyah, Qabab, Jishb [8, 10]

Brief botanical description: The largest aloe in Yemen, having an erect stem 2-3 m high. Leaves pale green, clustered at the top of the stem, pendulous 60-90 cm long, the marginal teeth white. Inflorescence erect, branched. Perianth red brown, glabrous, ca. 1 cm broad. Capsule cylindrical.

Flowering time: October - March.

Habitat: Widespread on steep rocky hills, between 600 -1800 m above sea level (a.s.l.)

Distribution in Yemen: Toor Al-Baha district, Taiz, Al-Qaeda, Hammam Ali, Wadi Hijan (Haraz), Hujela,

Hadhramout, near Ra's Huweira, Adhale [8, 13, 14].

Global distribution: Endemic to Arabian Peninsula: Yemen and Saudi Arabia [10]

Chemical constituents: The toxic piperidine alkaloids coniine, γ-coniceine, and the quaternary N, N-dimethylconiine (a minor component) were isolated from *A. sabaea* leaves growing in Taiz, Yemen, together with a new chlorinated natural product named N-4´-chlorobutylbutyramide, which was for the first time to be isolated from the Asphodelaceae family (published as Aloaceae) [15]. The 1,8-dihydroxyanthraquinones compounds, chrysophanol and asphodeline were detected in the roots of *A. sabaea* [16].

Ethnobotanical uses: The heated leaves are used locally for the treatment of tumors, bruises and spraining of ankle. In addition, the dry leaves are grazed little by livestock in the dry season. The plant is also used as firewood.

Pharmacological activity: The methanolic extract of the aerial part of *A. sabaea* was found inactive in the *in vitro* cytotoxic activity test, using Sulforhodamine B colorimetric assay, against four human cell lines, namely, a breast cancer cell line (MCF7), hepatocellular carcinoma cell line (HEPG2), cervix cancer cell line (HELA) and human normal melanocytes (HFB4) [17].

Aloe species were not generally known as toxic plants and the commercial trade in Aloe derived natural products is based mainly on two materials obtained from the leaves: Aloe exudate used as laxatives and derived from several Aloe species such as *A. ferox, A. marsabitensis, A. ngongensis, A. rabaiensis, A. scabrifolia* and *A. secundiflora* and aloe gel derived primarily from *A. vera* and used in products applied topically for skin ailments or taken internally for digestive complaints and general wellbeing [18]. However, death cases in rural Africa caused by infusions of three Aloe species, *A. chabaudii* Schönl., *A. globuligemma* Pole Evans and *A. ortholopha* Christian & Milne-Redh., drunk as an herbal medicine were reported [19]. Moreover, several toxic piperidine alkaloids were found in several Aloe species such as γ-coniceine and conhydrinone in *A. ballyii* Reynolds, γ-coniceine in *A. ruspoliana* Bake, *A. ibitiensis* Perrier and *A. gracilicaulis* Reynolds & P.R.O.Bally, γ-coniceine and pseudoconhydrine in *A. deltoideodonta* Baker, γ-coniceine and conhydrine in *A. gariepensis* Pillans and coniine and trace of γ-coniceine in *A. viguieri* Perrier [19]. Coniine and γ-coniceine were found to produce teratogenic effects such as multiple congenital contracture deformities in the offspring of pregnant cows dosed with plant that has high concentrations of either piperidine alkaloid [20]. Coniine and γ-coniceine were also reported to be associated with accidental and deliberate deaths in humans [21]. Consequently, campaigning for raising the public awareness against the use of *A. sabaea* plant by the people and livestock is required. Moreover, we emphasize the need for further scientific investigations of *A. sabaea* as limited data on its phytochemical constituents, pharmacological and toxicological activities were available.

***Crinum album* (Forssk.) (1837) Fig. 2**

Type: Yemen, Kusma.

Synonyms: *Amaryllus alba* Forssk. (1775); *Crinum yemense* Defl. ex Schweinf. (1889).

Vernacular names: Tuhaf, Sarf, Soraf [6, 8, 10]

Brief botanical description: Robust perennial with a large bulb. Leaves 10-15, linear- lanceolate, up to a meter or more long, weakly ascending, the margins often undulate. Inflorescence an umbel with up to 20 flowers, flowers pendulous, bell-shaped, 20-25 cm long with conspicuous white lobes and a long narrow tube. Fruit a globose capsule about 5 cm in diameter.

Flowering time: Not known.

Habitat: It grows on the escarpment, on the high plateau and open rocky places, it usually grows on high altitude mountain slopes, between 1074 - 3300 m a.s.l.

Distribution in Yemen: Toor Al-Baha district, Taiz, Shibam, Sumara, Wadi Dhahr, Kumaym (Al-Hadah), Ibb, Yesleh, Adhale, Damt, Wadi Shares, Khamer, Jabal Taa'ker, Jabal Nu'man [8, 13, 14].

Global distribution: Endemic to Arabian Peninsula: Yemen and Saudi Arabia [10].

Chemical constituents: Phytochemical investigations of the bulbs of *C. yemense* Defl ex Schwinf. (syn. *C. album* (Forssk.) Herb, collected from Ibb province, Yemen) have resulted in the isolation of the following alkaloids: A lycorine type alkaloid: (-)-Lycorine (narcissine, galanthidine, amarylline, bellamarine), crinine-type alkaloids: ambelline, (+)-bulbispermine, (+)-crinamine, (+)-6-hydroxycrinamine, yemenine A, yemenine B and yemenine C, phenanthridine alkaloid: trisphaeridine and haemanthamine-type alkaloid: vittatine [22]. In addition, (+)-Haemanthamine (3-epicrinamine) was obtained from the whole plant as well as undulatine (a crinine-type alkaloid) [23]. Other minor alkaloids such as yemensine has also been isolated from *Crinum yemense* Defl [24]. Moreover, non-alkaloidal constituents such as 6-hydroxy-2H-pyran-3-carbaldehyde, 1,1´- bis (1,1´-carboxyethyl) ether and benzoic acid and the known alkaloid haemanthamine were isolated from the Yemeni *C. yemense* Defl ex Schwinf bulbs [25].

Ethnobotanical uses: No data were available.

Pharmacological activity: It has been reported that the 80% methanolic extract of the bulbs of *C. yemense* Defl ex Schwinf. (syn. *C. album* (Forssk.) Herb, collected from Ibb province, Yemen) showed a potent inhibitory effect on the production of nitric oxide (NO) (implicated in physiological and pathological processes, such as vasodilation, nonspecific host defense, ischemia reperfusion injury, and chronic or acute inflammation) in lipopolysaccharide (LPS)-activated macrophages and the isolated alkaloids thereof, yemenine A, (+)-crinamine, (+)-6-hydroxycrinamine, and (-)-lycorine were found to exhibit inhibitory activity on NO production in LPS - activated macrophages with IC_{50} values of 4.9, 1.8, 5.4 and 2.5μM, respectively without cytotoxic effects in the MTT assay. Their inhibitory activities were more potent than that of guanidinoethyl disulfide, a selective inducible nitric oxide synthase (iNOS) inhibitor (IC_{50} =7.4 μM). Moreover, (iNOS) induction of LPS-activated macrophages was suppressed by the four alkaloid constituents closely related to their inhibitions of NO production. These results suggested that the four alkaloids inhibited NO production mainly due to their inhibitory activities against iNOS induction in LPS-activated macrophages [22]. The pyran derivative, 6-hydroxy-2*H*-pyran-3-carbaldehyde isolated from the Yemeni *C. yemense* bulbs was found to be potentially an effective inhibitor of melanin synthesis because it possesses a significant tyrosinase inhibitory activity with IC_{50} of 42,2 μM. This inhibitory activity was more potent than that of the positive standard kojic acid (IC_{50}=75,2 μM) tested in the same assay. Moreover, *C. yemense* Defl. bulbs contain another known tyrosinase inhibitor viz. benzoic acid, which is known to be a copper chelator [25].

The compound lycorine is the major active component from the Amaryllidaceae family plant and has been isolated from a

number of Crinum species including *C. yemense* Defl [22] Lycorine possesses multiple pharmacological effects, including *in vitro* and *in vivo* antitumor activity by different mechanisms, *in vivo* and *in vitro* antiangiogenesis and tumour cell-mediated vasculogenic mimicry, antivirus effects against HIV-1 virus, severe acute respiratory syndrome-associated corona virus (SARS-CoV), poliovirus, flaviviruses, human enterovirus 71 (EV71), and avian influenza virus H5N1, antibacterial activity against several *Saccharomyces cerevisiae* strains rho$^+$, rho$^-$, and mit$^+$, antiinflammation (antarthritic activity in various arthritis animal models, blocking LPS-induced production of pro-inflammatory mediators and decreasing LPS-induced mortality in mice, diminishing the pro-inflammatory factor calprotectin induced cytotoxicity), inhibition of acetylcholinesterase, suppression of ascorbic acid biosynthesis *in vitro* and *in vivo*, antimalarial activity (against *Plasmodium falciparum*), significantly abolishing the NTPDase and ecto-5-nucleotidase activities of the parasite (*Trichomonas vaginalis*) while the transcript levels of NTPDase A or B are not affected, control of circadian period length, exerts a choleretic effect and multiple biological functions, such as body temperature-lowering action, analgesia, and excitation of female animal's uterus. More interestingly, lycorine has very low toxicity to normal cells and normal bodies at an effective dose.[26] Accordingly, this plant and its constituents, which possess a wide range of beneficial activities and low toxicity, can be considered as a lead for future material for the treatment of several diseases. Taken the facts that genetic, geographical, and environmental factors may influence the quality and quantity of the active constituents of the same plant species, we therefore suggest that *Crinum album* (Forssk.) growing in Toor Al-Baha district, which has not been investigated yet, also deserves scientific investigations to reveal its chemical constituents, and biological activities.

***Euphorbia fractiflexa* S.Carter & J.R.I. Wood (1982) Fig. 2**

Type: Yemen (Wood 3256)

Brief botanical description: Spiny succulent shrub to 2½ m, lacking a trunk and much branched at ground level with numerous at first decumbent but finally ascending branches. Branches 3-angled, the angles broadly winged, the wings not lobed but bent backwards and forwards in zig-zag fashion. Spines paired, 10-15 mm long, the spine shields decurrent. Cyathia in pedunculate cymes at the top of the branches. Capsule glabrous, trigonous, rounded, ca. 7 mm diameter, red when ripe.

Flowering time: March-May

Habitat: An uncommon plant usually growing in colonies on gravel mounds, stony soils of coastal plains and rocky outcrops between 150-539 m a.s.l.

Distribution in Yemen: Toor Al-Baha district (Lahej), Haradh, Soq Al-Khamis, Abs (Tihama), Wadi Liyah, Tihama foothills [8, 13, 14].

Global distribution: Endemic to Arabian Peninsula: Yemen and Saudi Arabia [11].

Chemical constituents: No data were found.

Ethnobotanical uses: The plant is used to feed the camels. The latex is known by the local people to be caustic especially in the eyes.

Pharmacological activity: No data were available.

***Euphorbia fruticosa* Forssk. (1775) Fig. 2**

Type: Yemen (Schweinfurth 1361).

Vernacular name: Shurur [8].

Brief botanical description: Spiny succulent shrub to ca. 40 cm with 1-5, mostly unbranched stems arising from an underground base. Stems with 7-10 (-12) winged angles. Spines paired, 5-15 mm long, very numerous. Cyathia in sessile cymes at the top of the stems. Capsule on a decurved pedicel, glabrous, trigonous, rounded, ca. 3 mm diameter, becoming reddish with maturity.

Flowering time: January.

Habitat: Plants found on cliffs in the central escarpment and on stony plain between 1094-2200 m a.s.l.

Distribution in Yemen: Toor Al-Baha district (Lahej), South of Taiz, High altitude mountains, Haijah, Kuhlan, Khamer-Huth [8, 13, 14].

Global distribution: Endemic to Yemen [11]

Chemical constituents: Phytochemical screening of the succulent stems extracts of *Euphorbia fruticosa* (collected from Taiz province, Yemen) revealed the presence of flavonoids, sterols, and terpenoids [27].

Ethnobotanical uses: The whole plant is used in Yemen as antiparalytic [1]. The latex is considered by the local people to be caustic especially in the eyes. The dried plant is used to feed the camels and as firewood.

Pharmacological activity: The 80% ethanolic extract (5µg) of the *Euphorbia fruticosa* succulent stems (collected from Taiz province, Yemen) was found active against *Staphylococcus* aureus (Diameter of inhibition zone (DIZ) =14mm, comparing to the positive control methicilin (5µg) with DIZ of 19mm). In addition, the aqueous extract (5µg) of the latex was found to possess some activity (DIZ=16mm, comparing to the positive control nystatin (100 units) with DIZ of 27mm) against *Candida albicans* [28].

***Euphorbia inarticulata* Schweinf. (1899) Fig. 2**

Type: Yemen (Schweinfurth 1001).

Vernacular names: Suyayb, Qasas [8].

Brief botanical description: Much-branched, spiny succulent shrub to 2½ m, usually with a short trunk but often trunkless and with branches arising at ground level. Branches ascending, 3-5 angled, the angles slightly winged but not lobed. Spines paired, 5-15 mm long, the spine shields long, decurrent. Cyathia in sessile cymes at the top of the branches. Capsule glabrous, trigonous, rounded, ca. 3-4 mm diameter, purple-black when ripe.

Flowering time: November.

Habitat: It is growing on the escarpment and open stony ground from 300-2000 m a.s.l.

Distribution in Yemen: Widespread: Toor Al-Baha district, Tihama foothills, Western mountain, Taiz, Shara'b, Al-Hoban, Lahej, Abyan, Kuhlan Affar, Radaa, Huth, Damt, Qa'tabah, Adhale, Al-Husha, Guban, Dhisufal, Al-Qae'da, Assayani, Al-U'deyn, Al-Qafr, Mutheikhira [8, 13, 14].

Global distribution: Endemic to Arabian Peninsula: Yemen and Saudi Arabia [11].

Chemical constituents: No data were found.

Ethnobotanical uses: The latex, which is considered toxic, is used in Yemen against camel mange, and verruca [1]. The soft tips of the plant, after removing the latex, are eaten in rainy season. The dried plant is used to feed the camels and as firewood.

Pharmacological activity: No data were available.

***Euphorbia qarad* Defl. (1896) Fig. 2**
Type: Yemen (Deflers 296).
Vernacular names: Qasas, Hadel [13].
Brief botanical description: Spiny succulent shrub to 3 m with a distinct trunk. Branches very numerous. Spines paired, 5-10 mm long, the spine shields decurrent. Cyathia in pedunculate cymes at the top of the branches. Capsule on a recurved pedicel, glabrous, trigonous, rounded, deeply lobed, ca. 3-3.5 mm diameter.
Flowering time: May, June and August.
Habitat: It is growing on sandy plain at altitude of 250-665 m a.s.l.
Distribution in Yemen: Widespread: Toor Al-Baha district, Tihama foothills, Al Qala' village Bani Omer (South of Taiz), Bir Al Ahmer (Mawza). Wadi Allassbah (West of Taiz) [8, 13, 14].
Global distribution: Endemic to Yemen [11].
Chemical constituents: No data were found.
Ethnobotanical uses: The plant is described for the treatment of diabetes [29]. The latex is used in Yemen against camel mange, and verruca and considered to be toxic [1]. The dried plant is used to feed the camels and as firewood.
Pharmacological activity: No data were available.

***Euphorbia uzmuk S*. Carter & J. R. I. Wood (1982) Fig. 3**
Type: Yemen (Radcliffe-Smith & Henchie 4794 K).
Vernacular name: Uzmuq [8].
Brief botanical description: Unarmed succulent tree to 2½ m with a distinct dull-green barked trunk about 1m high, from the top of which arise numerous erect or ascending, glabrous, cylindrical branches. Leaves quickly deciduous. Cyathia in small cluster at the top of the branches, pubescent, glands very small, ca. 1 mm broad. Capsule on a recurved pedicel, thinly pubescent, globose, 9 mm diameter. Seeds ovoid, smooth.
Flowering time: November.
Habitat: It is growing on small colonies between 735-1300 m a.s.l., on the escarpment, in gullies and on hills with loose volcanic rocks.
Distribution in Yemen: Toor Al-Baha district, Hagdah, Maqbanah, and Hidhran (West of Taiz), Wusab As Safel: Al Mishrafa, Al Masbah and near suq Ar Rabu, Al Hujariya, An Nashama, Bani Assurur, As Safiah, Al Batheijah and Bani Umar, E, of Ibb [8, 13, 14].
Global distribution: Endemic to Yemen [8, 11].
Chemical constituents: Phytochemical screening of Yemeni *Euphorbia uzmuk* whole plant extracts (Ethyl acetate, methanol and aqueous) indicated the presence of flavonoids, saponins, sterols, terpenoids and tannins (Personal information from the first author).
Ethnobotanical uses: not known. The latex is known by the local people to be caustic especially in the eyes.
Pharmacological activity: The whole plant aqueous extract of *E. uzmuk* (5mg) was found to demonstrate antibacterial activity against *E. coli* (DIZ =13±1.5 mm) approaching those exhibited by the positive controls (Ampicillin (10µg), gentamicin (10µg) and erythromycin (15µg) with DIZ of 15±1, 17±1.5 and 13±1.5mm, respectively). The ethyl acetate extract also showed good antibacterial activity against *S. aureus* (DIZ = 13±1.2mm comparing to gentamicin (10µg) with DIZ of 19±1.5mm) and *S. epidermidis* (DIZ = 20±2mm comparing to gentamicin (10µg) with DIZ of 23±1.5mm) [27].
Although the Euphorbia genus has been extensively studied for its chemical constituents, pharmacological activities and medicinal uses [29-31] and there is a growing interest in the natural products from this genus, induced by the release of the drug Picato (a diterpene, ingenol mebutate, isolated from *Euphorbia peplus*) that has been approved by the U.S. Food and Drug Administration and by the European Medicines Agency for the topical treatment of actinic keratosis [32-33] only very few scientific investigations have been reported for *Euphorbia fruticosa* and *Euphorbia uzmuk* out of the five Euphorbia species of our study. Consequently, we emphasize the need for studying the Euphorbia species in Toor Al-Baha district to identify the species with valuable medicinal properties that could serve as a basis for the discovery of potential new natural product - based drug leads and to reveal the toxic species, as previous studies have indicated a number of Euphorbia spp. contain skin irritants, and cancer promoting compounds [34-41]. We therefore highlight the need to raise the public awareness against the use of the Euphorbia species as long as their efficacy and safety are not evaluated.

***Heliotropium longiflorum* (A. DC.) Jaub. & Spach (1852) var. *longiflorum* Fig. 3**
Type: Arabia: Saudi Arabia; Djebel Sidr (Mt. Sedder).
Synonym: *Heliophytum longiflorum* A. DC. (1845).
Vernacular name: Lasan Athour.
Brief botanical description: Erect strigosa perennial herb to 50 cm usually much branched and slightly woody below. Leaves entire, green, ovate-lanceolate. Inflorescence of scorpioid cymes, terminal, forked, slender, up to 20 cm long. Flowers rather small, calyx strigosa, minute, ca.1 mm long, divided almost to the base. Corolla white, ca. 5 mm long. Nutlets 4, glabrous.
Flowering time: Throughout the year.
Habitat: Common throughout the Tihama, escarpment and high plateau reaching 2300 m a.s.l. It grows in open habitats including fields, roadsides, wadi beds and rough grassland.
Distribution in Yemen: Toor Al-Baha district, Tuban district, Lahej, Tihama, Abyan, Al-Maraqisha, Yafea, Hadhramout, Taiz [8, 13, 14].
Global distribution: Endemic to Arabian Peninsula: Yemen and Saudi Arabia [14].
Chemical constituents: No data were available.
Ethnobotanical uses: Dried leaves are used by local people as a treatment for abscesses, pimples, torsion of joints, and animals' mange. The seeds are useful against snake's bites. The plant is grazed by livestock when it is green. In Ethiopia, the water extract of the leaves is used orally and nasally for the treatment of some common diseases such as febrile diseases [42], while in Randa region, Djibouti, the plant is used for teeth decays, treatment of infections and allergies [43].
Pharmacological activity: We did not find any scientific studies that address the pharmacological activities of the near endemic *Heliotropium longiflorum* (A. DC.) Jaub. & Spach var. *longiflorum* despite a number of studies revealed a wide range of pharmacological activities and various traditional medicinal uses of different parts of other *Heliotropium* species for the treatment of various diseases [44-48]. However, some species of the genus *Heliotropium* are very poisonous in nature due to presence of pyrrolizidine alkaloids. Human deaths were reported to be due to accidental consumption of these species in many countries. Liver damage was caused by pyrrolizidine alkaloids because they were responsible for hepatic-veno occlusive disease. Epidemics of pyrrolizidine poisoning have occurred in Afghanistan. The outbreak was caused by consumption of bread made from wheat contaminated with seeds of *Heliotropium* plants, which were shown to contain pyrrolizidine alkaloids [47, 49]. Ill-thrift,

ascites and degenerative lesions in the liver were the major findings in chickens and ducks fed a commercial poultry diet containing heliotrine and lasiocarpine. The source of these pyrrolizidine alkaloids was probably the seeds of *H. europaeum* harvested with wheat [50]. A mortality rate of 33% in mixed-breed cattle was recorded, following ingestion of hay contaminated with *H. europaeum* at a level of 12% dry weight. The toxicosis event was characterized by typical clinical and histopathological signs of pyrrolizidine alkaloids toxicosis [51]. Hepatic veno-occlusive disease in four young women who had taken an herbal tea as treatment for psoriasis was found to be due to pyrrolizidine alkaloids from *H. lasiocarpum* contained as an ingredient of the herbal mixture. The human toxicity of *H. lasiocarpum* has been known for many years, since it was recognised by Russian workers as the cause of an epidemic of liver disease in Uzbekistan, where it was consumed as a contaminant in grain [52]. In the light of the fact that worldwide many cases of severe and fatal hepatic intoxications were reported, which were caused by using herbal medicines or food containing pyrrolizidine alkaloids derived from Heliotropium species and due to the lack of any study of the near endemic *Heliotropium longiflorum* (A. DC.) Jaub. & Spach var. *longiflorum* growing in Toor Al- Baha district, we highlight the need to raise public awareness of the importance of avoiding the usage of this plant for humans and livestock until its phytochemical constituents, especially its pyrrolizidine alkaloids profile, pharmacological and toxicological activities have been investigated.

***Pavetta longiflora* Vahl subsp. *longiflora* Vahl (1794) Fig. 3**

Type: Yemen, Taiz (Forsskal 1559).

Synonym: *Pavetta arabica* Bremek (1934).

Vernacular names: Shawaaf, Shenaf, Bunain [9].

Brief botanical description: A leafy shrub up to ca. 1 m tall. Leaves opposite, petiolate, elliptic or oblong to lanceolate, up to 12 × 3.5 cm, glabrous. Inflorescence usually dense, the pedicels 4-11 mm long, calyx with very short triangular teeth up to 1.5-2 mm long, corolla white, tube, 1.5-2.5 mm long. The corolla and calyx glabrous or nearly so. Drupe globose ca. 8 mm across.

Flowering time: April, May and November.

Habitat: It is growing on cliffs between 645-1800 m a.s.l.

Distribution in Yemen: Toor Al-Baha district, Taiz, At Turba, J. Saber, Assayani, Al Qae'de, Ibb, Dhisufal, Al U'deyn, Rayma, Jihaf, Al Hus'ein, Ashue'ib, Adhale [8, 13, 14].

Global distribution: It is endemic to Arabian Peninsula: Yemen and Saudi Arabia [9].

Chemical constituents: No data were available.

Ethnobotanical uses: The leaves are used as antimalaria agent. They are also grazed little by goats and camels. The fruits are edible.

Pharmacological activity: A study of *Pavetta longiflora* Vahl. subsp. *longiflora* leaves, collected from Taiz province, Yemen, revealed that the dichloromethane extract exhibited an inhibitory effect (IC_{50} of 3.1µg/ml) on human neutrophil elastase (HNE) and it has been suggested that the plant could contain HNE inhibitory constituents that may possess antiinflammatory activity and might be able to target the destructive and inflammatory actions of human neutrophil elastase [53]. The antiinflammatory activity as well as the ethnobotanical use of the plant as antimalarial agent were supported by a number of studies that revealed related species such as *P. corymbosa* (DC.) F.N. Williams [54], *Pavetta schumanniana* F. Hoffm. ex K. Schum., [55] and *P. crassipes* K. Schum [54, 56, 57]. possess antimalarial activity. Moreover, the antimalarial properties of *Pavetta crassipes* were credited to the presence of alkaloids and flavonoids (such as quercetin 3-O-rutinoside) [58-60]. The antiinflammatory activity was reported for *Pavetta indica* Linn. Leaves, [61] and *Pavetta crassipes* leaves [62]. Furthermore, a number of other pharmacological activities were attributed to several *Pavetta* species and their isolated compounds, such as the antimicrobial activity [63-64], hypotensive activity [65], antileishmanial, antitrypanosomal and cytotoxic activities [57], anthelmintic activity [66], anticholinesterase, antidiabetic, antioxidant, and neuroprotection effects [67]. Consequently, *Pavetta longiflora* Vahl subsp. *longiflora* growing in Toor Al-Baha district needs to be studied phytochemically, pharmacologically and most importantly, toxicologically because two species of *Pavetta*, namely, *Pavetta schumanniana* and *Pavetta harborii* were reported to cause gousiekte, which is a cardiac syndrome that was found to cause the death of about 7000 head of livestock, mainly sheep, goats and cattle, each year in south Africa. The causal toxin is a polyamine, named pavettamine after the genus *Pavetta*, and its chemical structure was published in 2010 [68-69]. Therefore, we suggest educating the local people to avoid using this plant until its safety is elucidated.

***Tribulus macropterus* Boiss. var. *arabicus* (Hosni) Al-Hemaid & J. Thomas (1996) Fig. 3**

Type: Oman, West of Jabal Sumhan.

Synonyms: *Tribulus arabicus* Hosni (1977); *T. omanense* Hosni (1978).

Vernacular names: Zahr, Qayoob, Qatoob [7]

Brief botanical description: Prostrate or decumbent, woody-based subshrub, 50-100 cm tall. Stem and leaves villous with short appressed and long erect hairs. Larger leaves 2.5-5 cm long; smaller leaves 0.8-1.2 cm long; leaflets 4-6 × 2-3 mm, oblong-elliptic. Sepals lanceolate, acute. Petals obovate, pale to bright yellow. Stamens 10. Stigma linear, as long as or longer than style. Ovary densely hairs, with straight hairs. Fruit 1-1.5 cm wide, densely hairs between the wings, wings dentate or subentire, pubescent or sparsely pubescent.

Flowering time: It was found with flowers in February to April, also in November and December.

Habitat: It is growing on sand dunes, in sandy and saline soil between 212-439 m a.s.l.

Distribution in Yemen: Toor Al-Baha district, Tihama, Bir Ahmed, West Tuban [8, 13, 14].

Global distribution: Endemic to Arabian Peninsula: Saudi Arabia, United Arab Emirates, Qatar, Oman, and Yemen [7, 12].

Chemical constituents: Screening of *Tribulus macropterus var. arabicus*, collected from a valley around the UAE University campus in Al-Ain, United Arab Emirates, revealed positive results for alkaloids, flavonoids, tannins, cardiac glycosides and saponins [70]. In addition, the aerial part of *Tribulus macropterus* Boiss, collected from Jeddah-Saudi Arabia, was found to contain glycosides, flavonoids, tannins, triterpenes and saponins [71]. Five compounds, were isolated from the whole plant of *Tribulus macropterus* Boiss collected from Suez-Ismailia road, Egypt, and identified as: (22*S*,25*S*)-16*β*,22,26-trihydroxy-cholest-4-en-3-one-16-*O*-*β*-D glucopyranosyl-(1→3)-*β*-D-xylopyranoside, (22*S*,25*S*)-16*β*,22,26-trihydroxy-cholest-4-en-3-one 16-*O*- *β* -D-glucopyranosyl-(1→3)- *β* -D-glucopyranoside, sucrose, D-pinitol and 3*β*- hydroxy-5*α*-pregn-16(17)en-20-one-3-*O*-*β*-D-xylopyranosyl-(1→2)-[*β*-D-xylopyranosyl-(1→3)]-*β*-D glucopyranosyl-(1→4)-[*α*-L-rhamnopyranosyl-(1→2)]-*β*- D-

galactopyranoside [72].

Ethnobotanical uses: The whole plant is grazed by camels.

Pharmacological activity: Testing the antioxidant activity of *Tribulus macropterus var. arabicus* by using 1-1 diphenyl -2-picrylhydrazyl (DPPH), 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS), Ferric Reducing-Antioxidant Power (FRAP) and β-Carotene bleaching assays demonstrated that *Tribulus macropterus var. arabicus* showed DPPH and ABTS radical scavenging activities (43.9% and 88.0% inhibition at the maximum concentration of 1000 µg/ml, respectively) comparing to the positive standards ascorbic acid (60.55% at 300 µg/ml) and butylated hydroxytoluene (BHT) (51.5% inhibition at 32 µg/ml). The optical density (OD) value at 593 nm for the FRAP assay was found to be 0.138 and 0.48 for the control (0) and at 1000 µg/ml, respectively comparing to the standard ascorbic acid (0.129 and 0.399 for the control (0) and at 100 µg/ml, respectively), while the OD values at 470 nm for β-carotene bleaching assay was 0.190 and 0.229 for the control (0) and 1000 µg/ml, respectively [70]. *T. macropterus* Boiss collected from Jeddah, Saudi Arabia, was evaluated for the antihyperglycemic and antihyperlipidemic effects by oral administration of the methanolic extract of the aerial parts in streptozotocin induced diabetic rats at a dose of 500 mg/kg bodyweight. It has been revealed that the antihyperglycemic effect was manifested by the significant reduction of the fasting blood glucose level, started after the 3rd week of treatment and continued till the 4th week (31% and 30%, respectively). This result was in accordance with the reported data of the significant reduction of the level of serum glucose, after administration of saponin fraction isolated from *Tribulus terrestris*, by 26.25% and 40.67% in normal and diabetic mice, respectively. It was also demonstrated that pre-treatment of diabetic rats with methanolic extract induced an increase in glucose utilization and glucose tolerance. In addition, the extract may also reduce gluconeogenesis, which was approved after the determination of plasma level of insulin at the end of the experiment. Administration of the methanolic extract for 4 weeks was also found to significantly increase the insulin blood levels by 189.9%, which may be through stimulation of the activity of the remnant pancreatic β-cells. The hypolipidemic effect of the administration of methanolic extract for 4 weeks was demonstrated by a significant reduction in plasma total cholesterol by 37.2% and low-density lipoprotein cholesterol by 42.1% and increase of high-density lipoprotein cholesterol by 91.9%. Moreover, the methanolic extract of *T. macropterus* aerial parts was found safe with neither deaths reported in the rats treated with different doses of the extract nor presence of any apparent physical signs of drug-induced toxicity during the whole experimentation period [71]. The methanol extract of the whole parts of *Tribulus macropterus* Boiss collected from Suez-Ismailia road, Egypt, was found to demonstrate cytotoxic activity against a human tumor cell line (hepatocyte generation 2, HepG2) (IC_{50} = 2.9μg/ml). The *n*-butanolic fraction obtained from successive fractionation of the methanolic extract also exhibited activity against HepG2 (IC50 = 2.6 μg/ml). The three steroidal compounds isolated from the *n*-butanolic fraction, namely: (22*S*,25*S*)-16*β*,22,26-trihydroxy-cholest-4-en-3-one-16-*O*-*β*-D-glucopyranosyl-(1→3)-*β*-D-xylopyranoside, (22*S*,25*S*)-16*β*,22,26-trihydroxy-cholest-4-en-3-one-16-*O*- *β* -D-glucopyranosyl-(1→3)- *β* -D-glucopyranoside and 3*β*- hydroxy-5*α*-pregn-16(17)en-20-one-3-*O*-*β*-D-xylopyranosyl-(1→2)-[*β*-D-xylopyranosyl-(1→3)]-*β*-D-glucopyranosyl-(1→4)-[*α*-L-rhamnopyranosyl-(1→2)]-*β*- D-galactopyranoside were also found to demonstrate cytotoxic activity against the same cell line HepG2 and their IC_{50} values were 2.4, 2.2 and 1.1 μg/ml, respectively [72].

Tribulus macropterus Boiss. var. *arabicus* growing in Toor Al-Baha district has not yet been investigated. We stress the need for studying this plant species because the genus Tribulus has been shown to be rich in furostane-, cholestane- and spirostane-type steroidal saponins [73] that have displayed a wide range of biological activities, including cytotoxic, and antiproliferative activities [74]. Phytochemical investigations of *Tribulus* species also showed that the major constituents are steroidal glycosides followed by flavonoid compounds and alkaloids [72]. However, studying the safety of the plant is a priority as it was found that despite the significant medicinal value of the famous most studied species (*Tribulus terrestris*) in the traditional systems of medicine, viz. Ayurveda, Chinese, Siddha, and Unani and its reputation in the folk medicine of many countries for the treatment of male infertility and cardiac diseases among a number of other diseases as well as the exhaustively investigation of its phytochemical constituents and wide range of pharmacological activities [75-76], *Tribulus terrestris* toxicity were reported such as the case of hepatotoxicity, nephrotoxicity and neurotoxicity in an Iranian male patient who used the plant's extract to prevent kidney stone formation. The patient presented with seizure and very high serum aminotransferases and creatinine after consuming herbal water for 2 days [77], and another case of a severe hyperbilirubinemia followed by acute renal failure and bile containing casts in the tubules in a young healthy male after ingestion of the plant [78]. Moreover, grazing livestock on *Tribulus terrestris* and *Tribulus micrococcus* were found to be associated with sheep staggers (two locomotor disorders, chronic *Tribulus* staggers caused by *Tribulus terrestris* and transient *Tribulus* ataxia caused by *Tribulus micrococcus*, both of these nervous disorders are only recorded in New South Wales, Australia), and nitrate poisoning (usually seen only when hungry sheep or cattle are put into a paddock that has an abundant growth of *Tribulus terrestris* or *Tribulus micrococcus*) as well as hepatogenous photosensitisation commonly referred to as 'yellow big head' or geeldikkop (caused by a combination of the ingestion of a toxin from *Tribulus terrestris* and possibly a toxin produced by a pasture litter fungus called *Pithomyces chartarum* that results in liver damage and photosensitisation). This livestock toxicity leads to many fatalities of the animals [79-82]. *Tribulus terrestris* growing throughout Yemen was also recorded to be one of the major sources of toxicity of livestock especially in drought season when animals were predisposed to toxic plants by decreasing supplies of alternative feeds [83]. Accordingly, we emphasize the necessity for studying the effectiveness and the safety of *Tribulus macropterus* Boiss var. *arabicus* growing in Toor Al-Baha district.

Conclusions

This review provided scientific documentation, for the first time, of ten endemic and near endemic plants of Toor Al Baha district, Yemen. The outcomes of researching the scientific data of the selected plants have revealed the limited scientific investigations of their phytochemical constituents, pharmacological and toxicological properties. The phytochemical constituents were reported only for 5 plants, namely, *A. sabaea* leaves (toxic piperidine alkaloids and N-4´-chlorobutylbutyramide) [15], *C. album* bulbs (Alkaloidal and non-alkaloidal constituents) [22-25], *E. fruticose* succulent

stems (Flavonoids, sterols, and terpenoids) [27], *E. uzmuk* whole plant (Flavonoids, saponins, sterols, terpenoids and tannins) and *Tribulus macropterus* Boiss. var. *arabicus* (Alkaloids, flavonoids, tannins, cardiac glycosides and saponins) [70]. The pharmacological activities were demonstrated for 5 plants, *C. album* bulbs and its constituents (Inhibition of NO production by bulb extract and its alkaloids [22], inhibition of melanin synthesis by the pyran derivative [25], and multiple pharmacological effects of the compound lycorine [26]), *E. fruticose* succulent stems (Antimicrobial activity of the extract) [28], *E. uzmuk* whole plant (Antibacterial activity of the extract) [27], *Pavetta longiflora* Vahl subsp. *longiflora* leaves (inhibition of human neutrophil elastase by the extract) [53], and *Tribulus macropterus* var. *arabicus* (antioxidant activity) [70]. On the other hand, related species were found to possess a wide range of pharmacological activities as well as several toxicological properties. Consequently, this study emphasizes the importance of the selected plants as promising candidates for future scientific investigations on their phytochemical constituents, pharmacological and toxicological activities to identify their valuable medicinal properties that could serve as a basis for the discovery of potential new drugs and to evaluate their safety as one of these plants and their related species were found to contain toxic compounds such as piperidine alkaloids in *A. sabaea* and pyrrolizidine alkaloids in some Heliotropium spp., skin irritants, and cancer promoting compounds in a number of Euphorbia spp., pavettamine in two Pavetta spp. Moreover, this work supplies valuable information for the local authority and health professionals to raise the public awareness against the use of these plants as long as their safety is not proved.

Aloe sabaea

Crinum album

Euphorbia fractiflexa

Euphorbia fruticosa

Euphorbia inarticulate

Euphorbia qarad

Fig 2: *Aloe sabaea, Crinum album, Euphorbia fractiflexa, Euphorbia fruticosa, Euphorbia inarticulate,* and *Euphorbia qarad*

Euphorbia uzmuk

Heliotropium longiflorum var. *longiflorum*

Pavetta longiflora subsp. *longiflora*

Tribulus macropterus var. *arabicus*

Fig 3: *Euphorbia uzmuk, Heliotropium longiflorum* var. *longiflorum, Pavetta longiflora* subsp. *longiflora,* and *Tribulus macropterus* var. *arabicus*

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