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A review on phytochemical, pharmacological and ethnopharmacological aspects of genus *Trichodesma*

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The genus *Trichodesma* belongs to the family Boraginaceae. The plants of this genus are widely distributed in tropical and subtropical regions of Africa, Asia, and Australia. Phytochemically, scientific reports on *Trichodesma* species so far revealed more than one hundred compounds from this genus, including hydrocarbons, phenols, flavonoids, sterols, terpenes and alkaloids have been isolated or identified. Medicinally, various reported biological activities of *Trichodesma* such as antimicrobial, antiparasitic, cytotoxic, anti-infection, antioxidant, anti-inflammatory, anti-irritant, antidiarrheal, antispasmodic, antimalarial, analgesic, antipyretic, anti-diabetic, diuretic, and hepatoprotective effects were discussed in this review otherwise**.** Also, the ethnopharmacological effects of this genus were reviewed. Among all the *Trichodesma* species, *T. indicum* is regarded as the most important one regarding its pharmacological values. The volatile oil of *T. africanum* L. showed high antioxidant activity.

Keywords: Pharmacological properties, Phytoconstituents, Traditional uses, *Trichodesma* genus.

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Introduction

Trichodesma R.Br. is a genus of about 45 species known from tropical and subtropical regions of Africa, Asia, and Australia[1-4]. Brown described *Trichodesma* in 1810[5]. It belongs to the family Boraginaceae established by Jussieu[6]. The group comprises predominantly perennial herbs, a genus well defined by flowers with a deeply divided and strongly accrescent calyx, the absence of fomices, anthers usually with fairly long, soft hairs on the back and conspicuous long, linear, often twisted connectives produced above the thecae[5]. The name *Trichodesma* is derived from the Greek words, *thrix* or *trikhos* (hair), and *desme* (band or bundle) and alludes to the twisted hairs or awns that terminate the anthers. The species name is a reference to the relatively narrow leaves[5].

Morphologically, *Trichodesma* is characterized by the calathiform to broadly infundibular corolla with a short tube, naked throat and patent to reflexed lobes cuspidate at the apex. The stamens, typically exserted, have anthers usually pubescent outside that form a cone by long, aristate and spirally twisted appendages of the connective tissue[7].

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Pyrrolizidine alkaloids and triterpenoids are common secondary metabolites in Boraginaceae family and are widely isolated from several *Trichodesma* species[8-11].

Pharmacologically and phytochemically, only a few numbers of *Trichodesma* species have been reported including *T. indicum* (L.) R. Br., *T. zeylanicum* (Burm.f.) R. Br., *T. incanum* D. C., *T. ehrenbergii* Schweinf. ex Boiss., *T. amplexicaule Roth.*, *T. sedgwickianum* Bane and *T.africanum* L. Among all the *Trichodesma* species, *T. indicum* (L.) R. Br. is regarded as the most important one considering its pharmacological values according to literature[11-14]. Further studies are needed to investigate pharmacological and phytochemical aspects of the other species belonging to this genus. So, in continuation of the authors' research[15-17], the present review aims to provide a point of reference for researchers to carry out more studies about *Trichodesma* plants.

Methodology

The authors searched databases of PubMed, Scopus, ProQuest, IEEE Xplore, EBSCO, ACS Publications, and Taylor & Francis etc. to find the relevant pharmacological properties of *Trichodesma* species as well as the literature dealing with the active constituents and ecological aspects. Keywords used for this research were "*Trichodesma*", "pharmacology", "ecology", and

"phytochemistry". Data gathering from the mentioned databases was performed up to 31st November 2019 through the Egyptian Knowledge Bank (EKB) and Saudi Digital Library (SDL).

Ethnopharmacological aspects

Many *Trichodesma* plants have been used in traditional medicines throughout the world to treat common diseases, such as ear pain, intestinal worms, wounds, cough, fever, dysentery, and rheumatism. Available data about traditional uses of various species of *Trichodesma*, their local names, and plant parts used to treat human ailments by local practitioners are listed in Table 1[14,18-32].

Phytochemical constituents

Qualitative and quantitative analysis of *Trichodesma* species revealed the presence of many secondary metabolite's classes including alkaloids, steroids, flavonoids, phenolic acids, fatty acids, and hydrocarbons[31,33-38]. The categorization, structures, and sources of these compounds are listed in Tables 2-4.

Aminoacids

Amino acids are organic compounds that contain amine and carboxyl groups attached to the alpha-carbon atom, along with a side chain specific to each amino acid[39]. Amino acids are the structural units (monomers) that makeup proteins. Because of their biological significance, amino acids are important in nutrition and are commonly used in nutritional supplements, fertilizers, feed, and food technology. So far, twenty-two amino acids as free and protein amino acids with different ranges of concentrations were determined from *T. ehrenbergii* Schweinf. ex Boiss., *T. indicum* (L.) R. Br., and *T. Zeylanicum* (Burm.f.) R.Br as listed in Table 3[40-42]. Cysteine is the common amino acid in the *Trichodesma* species.

Essential oil constituents

Essential oils are complex mixtures of volatile constituents frequently containing 20-60 or more individual compounds[43]. Common classes of compounds found in essential oils include hydrocarbons, esters, oxides, lactones, alcohols, phenols, aldehydes and ketones. These components have been reported to be responsible for several bioactivities ascribed to essential oils[44]. Essential oils have been recognized as therapeutic agents and widely utilized as potent natural medicinal components of plants[45].

Volatile oil from the leaves of *T. africanum* L. collected from Palestine was extracted using microwave, ultrasonic, microwave-ultrasonic, and conventional hydrodistillation methods. Among the four extraction methods used, the microwave-ultrasonic method yielded the largest amount (1.8% v/w)[34].

Table 1 — Uses of *Trichodesma* species in folk medicines.

Species	Country	Part used	Ailments treated	Ref.
T. indicum (L.) R. Br.	India	LP	Ear pain and wounds	18
	India	RP	Dysentery, cough, cold, fever, anasarca and joint pain	19-22
	India	LRP	Tumour, snake-bite and urinary diseases	14
	India	WP	Arthritis, anorexia, dysentery, skin diseases, snake-bite, fever, as emollient and as a diuretic.	19, 23
	Pakistan	WP	Intestinal worms	24
T. zeylanicum (Burm.f.) R.Br.	Australia	LP	As emollient and as diuretic	25
	Tanzania	LP	Scalp fungal infection	25
	Nigeria	LP	Fever, scorpion bite and as analgesic	26
	South Africa, Zimbabwe, and Comoros	LP	Wound healing, as analgesic, stillbirth, cough and scabies	25
	India	LP	Wound healing	27-28
	India	LRP	Dysentery and rheumatism	18
T. physaloides (Fenzl) A. DC.	South Africa	Tubers	Treat schistosomiasis	29-30
T. amplexicaule Roth.	India	WP	As emollient and poultice	11
	India	RP	Reduce swellings and dysentry	11
T. africanum L.	India	WP	As mollient andiuretic	11
T. khasianum C. B.Clarke	Taiwan	LP	Ulcers, antihypertensive, promote digestion and improve flatulence	31
T. sedgwickianum Bane	India	WP	Emollient and poultice	32
		RP	Reduce swelling of joints and depurative	32

AP: Aerial parts; SP: Plant stems; WP: Whole plant; LP: Plant leaves; RP: Plant roots; LRP: Leaves and roots parts

Table 2 — Preliminary phytochemical screening of the *Trichodesma* species

	Alkaloid	Phenolic	Flavonoid	Terpenoid	Tannin	Saponin	Anthraquinones	Volatile oil	Ref
T. africanum L.	+	±	±	+	+	+	−	+	33
T. zeylanicum (Burm.f.) R.Br.	NA	+	+	NA	+	+	NA	NA	34
T. sedgwickianum Bane	+	+	NA	+	NA	+	NA	NA	35
T. ehrenbergii Schweinf. ex Boiss.	+	+	+	+	+	+	NA	−	36
T. indicum (L.) R. Br.	NA	+		+	+	+	NA	NA	37, 38
T. khasianum C.B.Clarke	NA	+	+	NA	NA	NA	NA	NA	31

NA = Not available; + = Present; − = Absent; ± = Weak

Table 3 — Free and protein amino acids identified from the *Trichodesma* species.

Amino acid	*T. ehrenbergii* Schweinf. ex Boiss.	*T.indicum* (L.) R. Br.	*T. zeylanicum* (Burm.f.) R.Br.
Aspartic acid	+	+	-
Threonine	+	+	-
Serine	+	-	-
Glutamic acid	+	+	-
Proline	+	+	-
Hydroxy proline	-	-	-
Glycine	+	-	+
Alanine	+	-	-
Cysteine	+	+	+
Valine	+	+	-
Methionine	+	-	-
Isoleucine	+	-	-
Leucine	+	-	-
Tyrosine	+	-	+
Phenyl alanine	+	-	-
Lysine	+	-	-
Histidine	+	-	-
Arginine	+	-	-
Cystine	-	+	-
Amino n-butyric acid	-	+	+
Ornithine	-	-	+
Tryptophan	-	+	-
References	37	41-42	41

+ = Present; - = Absent

Fatty acids and hydrocarbons

A fatty acid is a carboxylic acid consisting of a hydrocarbon chain and a terminal carboxyl group, especially any of those occurring as esters in fats and oils. Most naturally occurring fatty acids have an unbranched chain of an even number of carbon atoms, from 4 to 28[46]. Phospholipids and triglycerides are the main precursors of fatty acids[47]. Twenty fatty acids, ester, and hydrocarbons identified from *Trichodesma* genus are summarized in Table 4[48-55]. The structure of identified fatty acids and hydrocarbons is shown in Fig. 1.

Phenolics and flavonoids

Phenolic compounds are a group of small molecules characterized by their structures having at least one phenol unit. Based on their chemical structures, phenolic compounds can be divided into different subgroups, such as phenolic acids, flavonoids, tannins, coumarins, lignans, quinones, and curcuminoids[56]. Phenolic compounds and flavonoids are widely distributed in nature and are the most abundant antioxidants in the diet, being the common components of fruits, vegetables, and their derivatives[57-58]. So far twenty-seven phenolics and flavonoids have been reported in various

Table 4 — Chemical constituents identified from *Trichodesma* species.

Compound	Species	References
	Fatty acids and hydrocarbons	
n-Decanyl laurate	*T. indicum* (L.) R. Br.	48
n-Tetradecanyl laurate	*T. indicum* (L.) R. Br.	48
n-Nonacosanyl palmitate	*T. indicum* (L.) R. Br.	48
n-Pentacos-9-one	*T. indicum* (L.) R. Br.	48
n-Dotriacont-9-one-13-ene	*T. indicum* (L.) R. Br.	48
Hexacosane	*T. indicum* (L.) R. Br.	49
	T. amplexicaule Roth.	50
Ethyl hexacosanoate	*T. indicum* (L.) R. Br.	51
21, 24-Hexacosadienoic acid	*T. indicum* (L.) R. Br.	51
Oleic acid	*T. indicum* (L.) R. Br.	51
	T. zeylanicum (Burm.f.) R.Br.	52
Linoleic acid	*T. indicum* (L.) R. Br.	53
	T. zeylanicum (Burm.f.) R.Br.	52
Palmitic acid	*T. indicum* (L.) R. Br.	53
	T. zeylanicum (Burm.f.) R.Br.	52
Stearic acid	*T. indicum* (L.) R. Br.	53
	T. zeylanicum (Burm.f.) R.Br.	52
Linolenic acid	*T. indicum* (L.) R. Br.	53
	T. zeylanicum (Burm.f.) R.Br.	54
	T. calcarata Batt.	55
Lauric acid	*T. zeylanicum* (Burm.f.) R.Br.	52
Malvalic acid	*T. zeylanicum* (Burm.f.) R.Br.	52
Hexacosanoic acid	*T. amplexicaule* Roth.	50
Ceryl alcohol	*T. amplexicaule* Roth.	50
Ricinoleic acid	*T. zeylanicum* (Burm.f.) R.Br.	52
Myristic acid	*T. zeylanicum* (Burm.f.) R.Br.	52
Sterculic acid	*T. zeylanicum* (Burm.f.) R.Br.	52
Phenolic acids and flavonoids		
Ferulic acid	*T. ehrenbergii* Schweinf. ex Boiss.	37
	T. khasianum C.B.Clarke	31
Gallic acid	*T. ehrenbergii* Schweinf. ex Boiss.	37
	T. indicum (L.) R. Br.	59
	T. sedgwickianum Bane	36
	T. africanum (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
	T. khasianum C.B.Clarke	31
Ellgaic acid	*T. ehrenbergii* Schweinf. ex Boiss.	37
Rosmarinic acid	*T. khasianum* C.B.Clarke	31
Protocatechuic acid	*T. khasianum* C.B.Clarke	31
Gentisic acid	*T. khasianum* C.B.Clarke	31
Chlorogenic acid	*T. khasianum* C.B.Clarke	31
Caffeic acid	*T. khasianum* C.B.Clarke	31
Syringic acid	*T. khasianum* C.B.Clarke	31
p-Coumaric acid	*T. khasianum* C.B.Clarke	31
Salicylic acid	*T. khasianum* C.B.Clarke	31
Quercitrin	*T. ehrenbergii* Schweinf. ex Boiss.	37
Naringenin	*T. khasianum* C.B.Clarke	31
Rutin	*T. khasianum* C.B.Clarke	31
Astralgalin	*T. ehrenbergii* Schweinf. ex Boiss.	37
Cynaroside	*T. ehrenbergii* Schweinf. ex Boiss.	37
Epicatechin	*T. ehrenbergii* Schweinf. ex Boiss.	37
	T. khasianum C.B.Clarke	31

(*Contd*.)

Table 4 — Chemical constituents identified from *Trichodesma* species.

Compound	Species	References
Catechin	*T. indicum* (L.) R. Br.	61
	T. sedgwickianum Bane	36
Quercetin	*T. ehrenbergii* Schweinf. ex Boiss.	37
	T. khasianum C. B. Clarke	31
	T. africanum (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
Kaempferol	*T. ehrenbergii* Schweinf. ex Boiss.	37
Luteolin	*T. ehrenbergii* Schweinf. ex Boiss.	37
Luteolin 7-O-*α*-L rhamnosyl (1-6)*β*-D-glucoside	*T. africanum* (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
Luteolin-7-diglucoside	*T. africanum* (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
Apigenin	*T. africanum* (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
6-Hydroxy-4'-methoxy aurone	*T. ehrenbergii* Schweinf. ex Boiss.	37
Umbelliferone	*T. africanum* (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
Scopoletin	*T. africanum* (L.) R. Br. *Var. heterotrichum* Bornm and Kneuck	60
Terpenoid		
β-Amyrin	*T. africanum* L.	64
α-Amyrin	*T. amplexicaule* Roth.	50
	T. indicum (L.) R. Br.	51
β-Methyl oleanate	*T. africanum* L.	64
Steroid		
β-Sitosterol	*T. Indicum* (L.) R. Br.	61
	T. Africanum L.	64
	T. Amplexicaule Roth.	50
	T. Indicum (L.) R. Br.	51, 36
	T. Sedgwickianum Bane	36
Stigmasterol	*T. Africanum* L.	64
Stigmast-5-en-3*β*-ol-23-one	*T. Indicum* (L.) R. Br.	48
Stigmast-5-en-3 *β*-ol-21(24)-olide	*T. Indicum* (L.) R. Br.	48
Lanast-5-en-3*β*-D-glucopyranosyl-21(24)-olide	*T. Indicum* (L.) R. Br.	48, 68
Lupeol	*T. amplexicaule* Roth.	50
	T. indicum (L.) R. Br.	69
Alkaloid		
Viridiflorine	*T. africanum* L.	77
Intermedine	*T. africanum* L.	77
Lycopsamine	*T. africanum* L.	77
Retronecine	*T. africanum* L.	77
	T. incanum D. C.	78
Trichodesmine	*T. incanum* D. C.	78-79
	T. africanum L.	80-81, 64
Europine	*T. africanum* L.	80-83
	*T. indicum (*L.) R. Br.	80-83
Monocrotolin	*T. indicum* (L.) R. Br.	69, 84
Supinine	*T. ehrenbergii* Schweinf. ex Boiss.	85
	T. indicum (L.) R. Br.	83
Senkirkine	*T. ehrenbergii* Schweinf. ex Boiss.	85
Incanine	*T. incanum* D. C.	79, 86
Quinine	*T. incanum* D. C.	78
Heliotrine	*T. indicum* (L.) R. Br.	83
Echimidine	*T. indicum* (L.) R. Br.	83

species of *Trichodesma*. The whole description of these compounds can be found in Table 4[31,36-37,59-61] and their structures are shown in Fig. 2.

Terpenoids

Terpenoids, the largest family of natural products with more than 40,000 structures, refer to a large class of

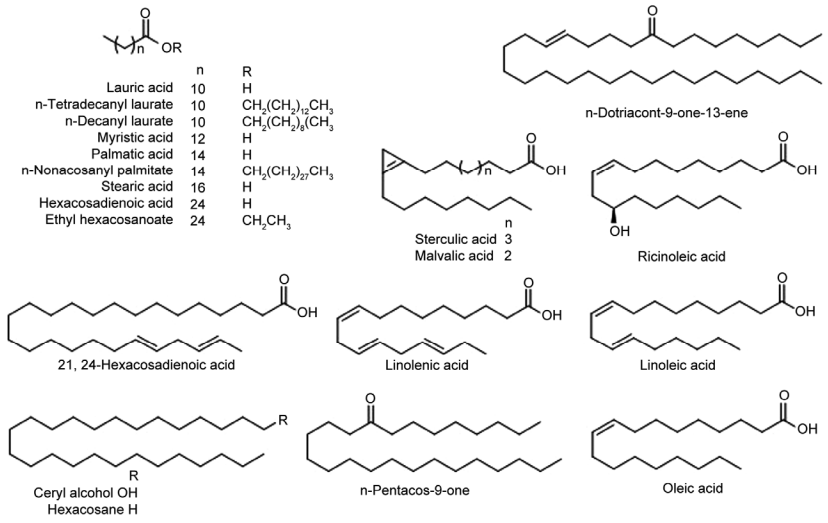

Fig. 1 — Chemical structure of fatty acids and hydrocarbons identified from *Trichodesma* species.

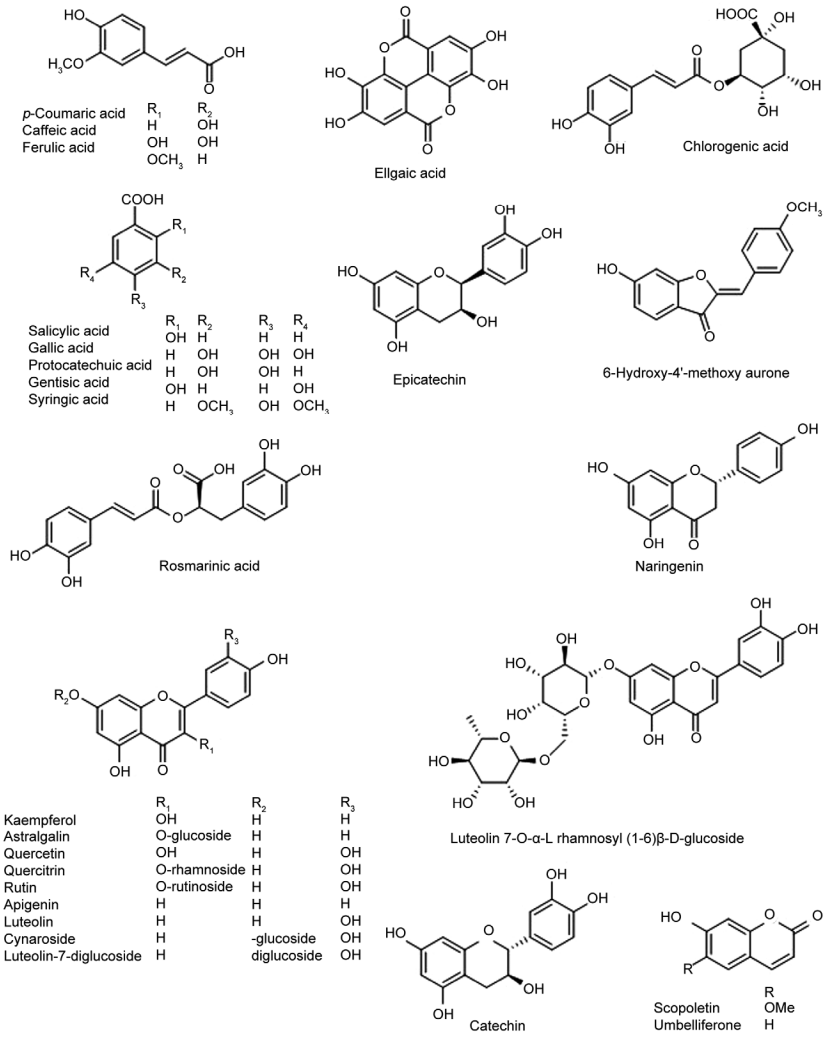

Fig. 2 — Chemical structure of phenolic, flavonoid and coumarin compounds isolated from *Trichodesma* species.

oxygen-containing terpene analogues that can be found in all classes of living things. Like terpenes, they are all derived from five-carbon isoprene units assembled and modified in different ways[62]. Terpenoids can be widely found in plants, which are responsible for the scents, flavours, and even colours in many plants[63]. So far three terpenoid compounds namely *α*-amyrin, *β*-amyrin, and *β*-methyl oleanate were isolated from *T. africanum* L., *T. amplexicaule* Roth. and *T. indicum* (L.) R. Br[50-51,64]. The structure of isolated terpenoids is shown in Fig. 3.

Steroids

A steroid is a biologically active organic compound with four rings (three six-member and one five-member) arranged in a specific molecular configuration. Squalene is the biochemical precursor to the whole family of steroids. Among all the steroid biosynthesis, steroid hormone biosynthesis is the most concerned[65-67]. Six steroids isolated from *Trichodesma* species are listed in Table 4[36,48,50-51,61,64,68-69] and their structure is shown in Fig. 4.

Alkaloids

An alkaloid has been defined by Pelletier as "a cyclic organic compound containing nitrogen in a negative oxidation state which is of limited distribution among living organisms"[70]. Various amino acids molecules are often their precursors[71]. Alkaloids have a wide range of pharmacological activities including antimalarial, antiasthma, anticancer, cholinomimetic, vasodilatory, antiarrhythmic, analgesic, antibacterial, and antihyperglycemic activities[72-76]. Pyrrolizidine alkaloids have been common in subfamilies of the Boraginaceae family and are widely isolated from a few species of

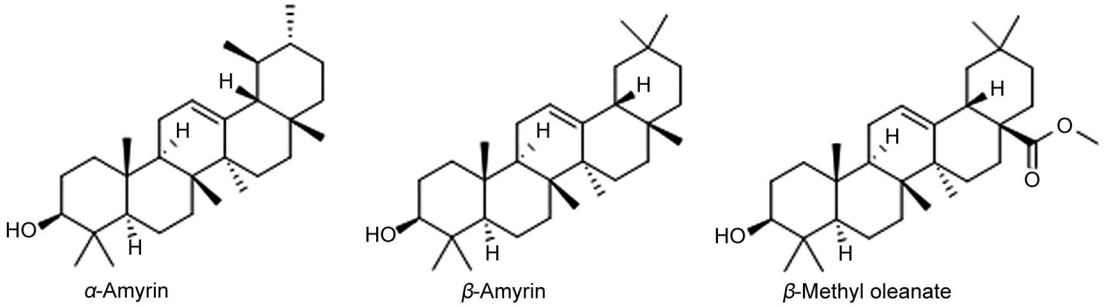

Fig. 3 — Chemical structure of terpenoid compounds isolated from *Trichodesma* species.

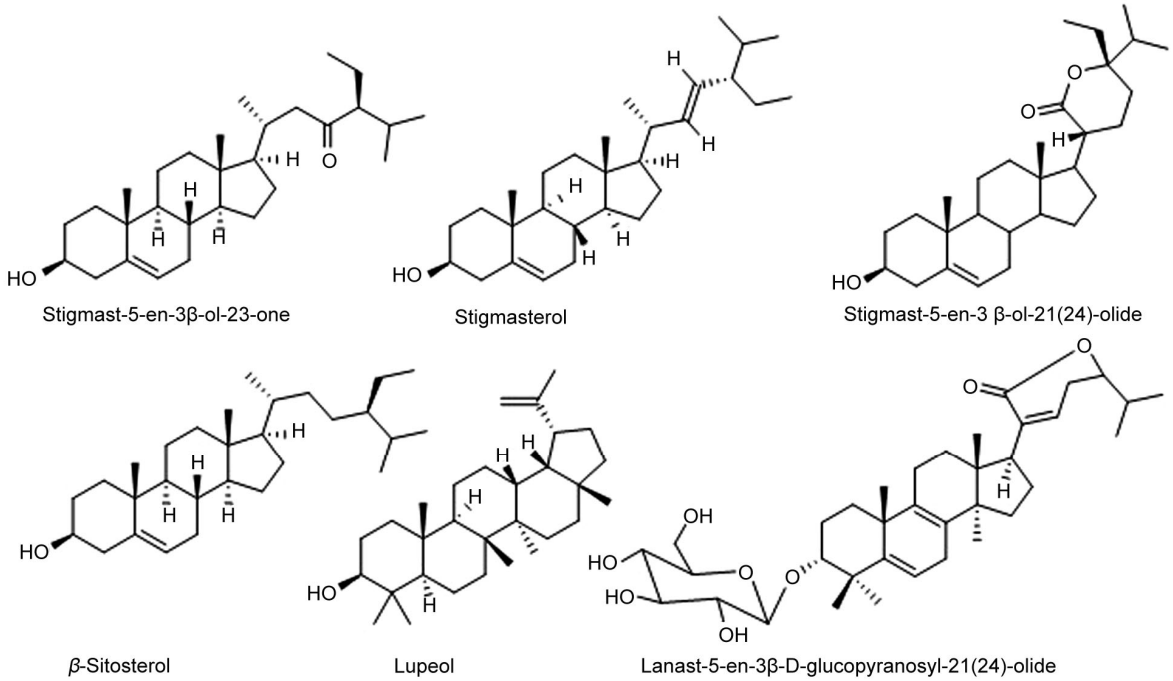

Fig. 4 — Chemical structure of steroid compounds isolated from *Trichodesma* species.

Trichodesma. Thirteen alkaloid compounds were isolated from *Trichodesma* species. The isolated alkaloids are listed in Table 4[64,69,77-86] and their structure is shown in Fig. 5.

Pharmacological effect

Pharmacology is the study of the interactions that occur between a living organism and chemicals that affect normal or abnormal biochemical function. If substances have medicinal properties, they are considered pharmaceuticals[87].

Antimicrobial activity

Antimicrobial activity refers to the process of killing or inhibiting the disease-causing microbes. Various antimicrobial agents are used for this purpose. Antimicrobial may be anti-bacterial, anti-fungal or antiviral. They all have different modes of action by which they act to suppress the infection.

Antimicrobial activity of *T. sedgwickianum* Bane[25,36], *T. africanum* (L.) R. Br. *var. heterotrichum* Bornm and Kneuck[60], *T. amplexicaule* Roth.[50], *T. indicum* (L.) R. Br.[48,59,88,89], *T. africanum* L.[90], and *T. ehrenbergii* Schweinf. ex Boiss.[91] was investigated by various known methods like disk-diffusion, broth or agar dilution etc. The inhibition zone and the minimum inhibitory concentration (MIC) were determined for various concentrations of each plant extract. Almost all these species showed fair to high antimicrobial activity against various gram-positive and gram-negative bacterial and fungal strains. Also, the volatile oil of *T. africanum* L. exhibited significant antimicrobial activities with MIC for *Escherichia coli*, *Pseudomonas aeruginosa,*

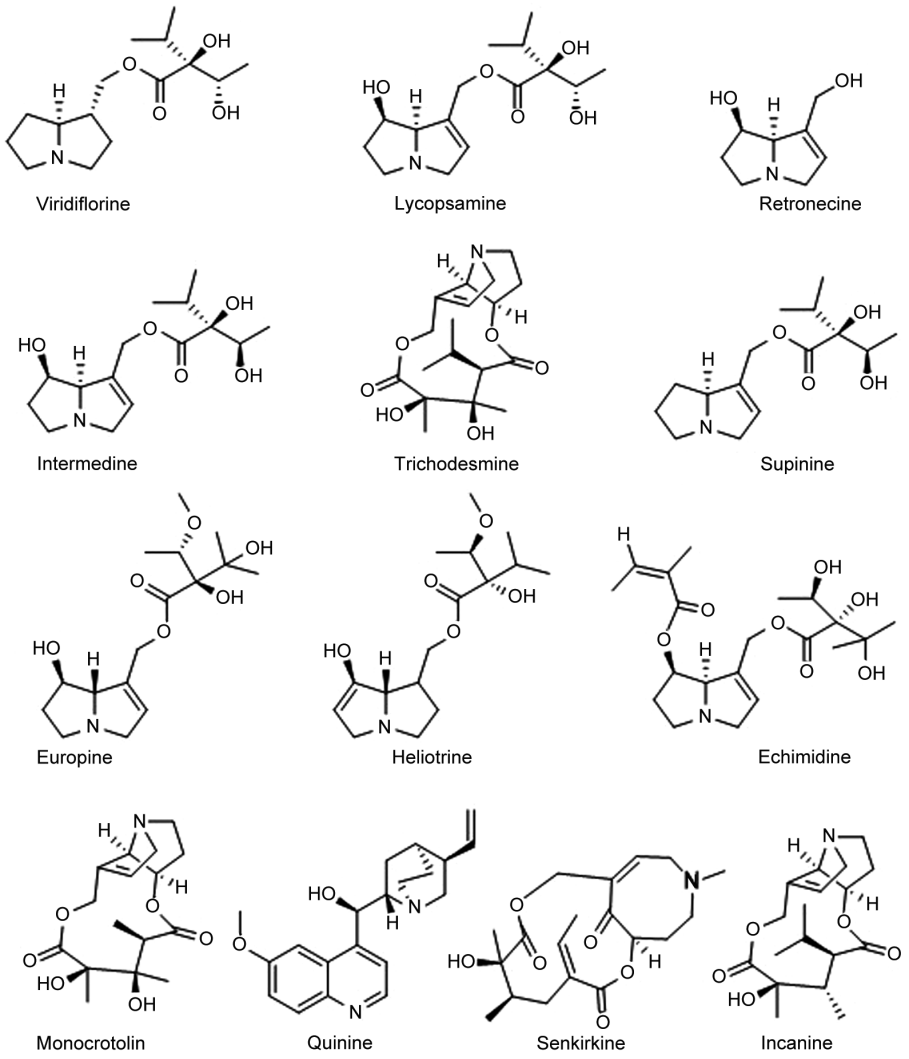

Fig. 5 — Chemical structure of alkaloid compounds isolated from *Trichodesma* species.

Staphylococcus aureus, and *Candida albicans* were 3, 5, 6, 3, and 9, respectively[34].

Antiparasitic activity

Antiparasitics are a class of medications that are indicated for the treatment of parasitic diseases, such as those caused by helminths[92], amoeba[93], ectoparasites, parasitic fungi[94], and protozoa[92], among others. Antiparasitics target the parasitic agents of the infections by destroying them or inhibiting their growth; they are usually effective against a limited number of parasites within a particular class. Antiparasitics are one of the antimicrobial drugs which include antibiotics that target bacteria, and anti-fungal that target fungi. They may be administered orally, intravenously or topically.

In vitro bioassay screening of methanol extracts of *T. africanum* L. growing in Egypt, was carried out for schistosomicidal activity. The extract was bioassayed at 100 µg/mL on viable *Schistosoma mansoni* mature worms in a culture medium. The viability of worms was examined after exposure for 24 h, and mortality was determined. *T. africanum* L. was found to possess weak reproducible in an *in vitro* antischistosomal activity[95].

Cytotoxicity activity

Cytotoxic agents are a substance used in the treatment of malignant and other diseases. They are designed to destroy rapidly growing cancer cells. They have been shown to be mutagenic, carcinogenic and/or teratogenic, either in treatment doses or animal and bacterial assays[96].

The cytotoxic activity of *Trichodesma* species was studied by one of the most well-known techniques 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) or lactate dehydrogenase (LDH) and the half-maximal inhibitory concentration (IC_{50}) was calculated.

T. africanum L. and *T. trichodesmoides* var. *tomentosum* R. Mill. showed no cytotoxic activity against MRC-5 (IC_{50}> 64)[97], also, *T. ehrenbergii* Schweinf. ex Boiss. showed weak cytotoxicity against liver carcinoma cell line (HEPG-2) and lung carcinoma cell (A-549) with IC_{50} 38.4 and 55.6 µg/mL, respectively[37], furthermore, the hydroalcoholic extract of the whole plant of *T. indicum* (L.) R. Br. exhibited poor cytotoxic properties against L6 Cell Line[98]. On the other hand, *T. africanum* L. aerial parts, given at different dose levels (300, 75 mg/kg/day) indicated that the plant extracts are toxic and lethal to Wistar rats by whatever route (oral or intramuscular) it was given[64,99]. Generally, *Tricodesma* showed no cytotoxic activity.

Anti-infection activity

Infections caused by protozoa such as *Trypanosoma*, *Plasmodium*, and *Leishmania* are a major worldwide health problem causing significant morbidity and mortality in Africa, Asia, and Latin America. Malaria kills between one and two million people annually, the majority of those affected being children under the age of five and pregnant women[100].

T. Africanum L. and *T. trichodesmoides* var. *tomentosum* R. Mill. showed non-significant as antimalarial, antitrypanosomal against *Trypanosoma brucei* (IC_{50} 32 and >64) and *Trypanosoma cruzi* (IC_{50}> 64 and 29), and Antiplasmodial against *Plasmodium falciparum* (IC_{50} 32 and 25), respectively[97]. Also, *T. africana, T. africanum* L., and *T. trichodesmoides* var. *tomentosum* R. Mill. were non-significant as antileishmanial against *Leishmania infantum*[97] and *Leishmania major*[101] with IC_{50} between 43-64. The reported *Tricodesma* species were non-significant as antimalarial, antitrypanosomal, antiplasmodial and antileishmanial.

Antioxidant activity

Most foods are made up of several organic compounds that can easily undergo oxidation. Lipids (such as fats, oils, and waxes) in general have the greatest tendency to lose electrons. Antioxidants were used to prevent the oxidation process in foods which lead to rancidity and browning, DNA oxidation and have many positive physiological effects in human[102]. Various antioxidants are supplied to the human body through diet, both vegetarian as well as non-vegetarian. Vitamins C and E, *β*-carotene and coenzyme Q are the most common antioxidants of diet[103-105]. The most promising methods used to evaluate antioxidant properties are DPPH (2,2-Diphenyl-1-picrylhydrazyl) scavenging method[106] and ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)).

Antioxidant activity of many *Trichodesma* species (*T. sedgwickianum Bane*[36], *T. trichodesmoides Gürke*[107], *T. indicum (L.) R. Br.* [61,98,108], *T. khasianum* C. B. Clarke[31], *T. zeylanicum* (Burm.f.) R.Br.[35], *T. amplexicaule* Roth.[109] from different countries was assayed by free radical scavenging by ABTS, DPPH, and nitric oxide and superoxide radical methods. The volatile oil of *T. africanum* L. exhibited antioxidant activity in terms of inhibition (91.83%±1.1)[34]. So far, *Trichodesma* species have revealed weak to good antioxidant effect.

Anti-inflammatory activity

Inflammation is a typical reaction by vascular tissues in biological systems against dangerous

external stimuli, such as an attack of a pathogen, irritants that lead to local accumulation of plasma, blood cells, and damaged cells. It is the resistance offered by the organism against any external factor causing damage, and it then heals any injury that occurred in any tissue[71].

It has been reported that a *T. indicum* (L.) R. Br. root extract has anti-inflammatory activity against histamine and serotonin-induced oedema in rats[48]. In addition, *T. amplexicaule* Roth. showed dramatic anti-inflammatory effects in the suppression of carrageenan-induced acute arthritis and complete Freund's adjuvant (CFA)-induced chronic arthritis in rats[110]. Moreover, *T. khasianum* C. B. Clarke dramatically decreased the protein levels of pro-inflammatory mediators such as inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), NO (nitric oxide), and prostaglandin E2 (PGE2) in a dose-dependent manner in lipopolysaccharide (LPS)-treated RAW264.7 macrophages[31]. *Trichodesma* had a dramatically anti-inflammatory effect.

Anti-irritant/anti-sting activity

Anti-irritants, whether naturally occurring or man-made, are substances that provide a soothing effect to irritated skin and reduce damage by a variety of mechanisms, including reduced absorption and/or biochemical manipulation of noxious chemicals[111].

Topical application revealed that *T. lanicum* seed extract reduces or eliminates the irritation or sting induced by the topical application of hydroxy acids (HAS) and/or retinoids. *T. lanicum* seed extract is claimed as an anti-irritant/anti-sting agent due to it contains cosmetic compounds likes hydroxy acids and/or retinoids and further compounds[112-113].

Antidiarrheal activity

Antidiarrheals are the name given to certain types of medicines that stop or slow diarrhoea. Antidiarrheals only relieve the symptoms of diarrhoea, such as an increased frequency and urgency when passing stools, they do not eliminate the cause of it.

The ethanolic extract of *T. indicum* (L.) R. Br. roots significantly inhibited the castor oil-induced diarrhoea in rats and decrease the propulsion of charcoal meal through the gastrointestinal tract. It also reduced the castor oil-induced small intestinal fluid accumulation. The root of *T. indicum* (L.) R. Br. has significant antidiarrheal activity and proves the use of this herbal remedy as nonspecific treatment of diarrhoea in folk medicine[114].

Antispasmodic activity

Antispasmodic compounds are currently used to reduce anxiety, emotional, and musculoskeletal tension, and irritability. Although most of the available antispasmodic compounds are synthetic or semisynthetic, traditional uses of this group of compounds are still popular[115]. The water extract of the leaves of *T. africana* from the United Arab Emirates (UAE) showed an inhibitory action on the spontaneous contractions of rabbit jejunal tissue, indicating antispasmodic activity with an IC_{50} 12.53 mg/mL and the percentage of maximum inhibition I_{max} was 61[(Ref. 116)].

Antidiabetic activity

Diabetes is a group of metabolic disorders characterized by a high blood sugar level over a prolonged time. Symptoms often include frequent urination, increased thirst, and increased appetite. If left untreated, diabetes can cause many complications. Antidiabetic agents aim to reduce blood sugar levels to an acceptable range and relieve symptoms of diabetes such as thirst, excessive urination, and ketoacidosis. Antidiabetic agents also prevent the development of or slow the progression of, long-term complications of the disease, such as nephropathy, neuropathy, and retinopathy.

Antidiabetic effect of the hydroalcoholic extract of the whole plant of *T. indicum* (L.) R. Br. was studied using the glucose uptake model in rodent skeletal muscle cells (L-6 cells) involved in glucose utilization. *T. indicum* (L.) R. Br. extract exhibited moderate antidiabetic activity[98]. Also, the methanolic extract of the plant leaves showed moderate α-amylase inhibitory activity (IC_{50}= 91.3 µg/mL). Almost all the tested extracts prominently reduce blood glucose levels in streptozotocin (STZ)-nicotinamide induced Type 2 diabetic rats. The methanolic extract has shown an estimable decrease of blood glucose level (P <0.01) along with glibenclamide. The results confirmed the anti-diabetic property of the plant extract against Type 2 diabetes mellitus[117].

Diuretic activity

Diuretic compounds that stimulate the excretion of water are potentially useful in most disorders including those exhibiting oedemata such as congestive heart failure, nephritis, toxemia of pregnancy, premenstrual tension and hypertension. Some of the diuretics are derived from medicinal plants[118].

Methanol and aqueous extracts of aerial parts of *T. indicum* (L.) R. Br. (150 and 300 mg/kg) were used

for screening diuretic activity using the Lipschitz model. The urine volume of the methanolic extract at a dose of 300 mg/kg has significant diuretic activity ($P \leq 0.001$) with Lipschitz value 1.25 as compared to standard (Furosemide). Urinary sodium concentration was found to be more in methanol extract, but potassium was found to be more in aqueous extract. It also shows methanol extract has an effect like K^+ sparing diuretics[119].

Hepatoprotective activity

The liver performs the normal metabolic homeostasis of the body as well as biotransformation, detoxification and excretion of many endogenous and exogenous compounds, including pharmaceutical and environmental chemicals. Drug-induced hepatotoxicity is a major cause of iatrogenic diseases, accounting for one in 600 to one in 3500 of all hospital admissions. There is a lack of reliable hepatoprotective drugs in modern medicine to prevent and treat drug-induced liver damage[120].

T. sedgwickianum Bane and *T. ehrenbergii* Schweinf. ex Boiss. demonstrated hepatoprotective activity by reducing the carbon tetrachloride-induced elevated level of various liver enzymes. These plants revealed potent hepatoprotective activity against the toxic effect of carbon tetrachloride comparable to the silymarin treated group[36-37].

Analgesic and antipyretic activity

Analgesic and antipyretic activities are commonly mentioned as characteristics of drugs that have an inhibitory effect on prostaglandin biosynthesis. The possible analgesic and antipyretic potential of the plant were studied using several experimental models.

The analgesic activity was determined in chemicals (acetic acid and formalin) as well as thermal (tail immersion) pain models in mice using classical standard drugs. The ethanol extract at doses of 100, 200, and 400 mg/kg exhibited a significant ($P < 0.001$) inhibition of acetic acid-induced abdominal constrictions in the mouse. In the tail immersion models, the extract (400 mg/kg) showed a significant increase ($P < 0.001$) in pain threshold to the meal stimulus and also in both the phase (early and late phase) of the hyper analgesic mode of formalin test[121].

The ethanolic extract of 400 mg/kg significantly inhibited both phases of the hyperalgesic mode of the formalin test and produced less effect in the first and more in the second phase. A rectal temperature was reduced up to 3 hours after administration in rats. The extract also reduced the rectal temperature in rats in yeast induced pyrexia for up to 4 hours after the administration and the efficacy produced was similar to that of standard drug. The results suggested that the extracts of different dose levels showed analgesic and antipyretic activity[121].

Conclusion

Plants of the genus *Trichodesma* have many bioactive constituents, many of which have been used in traditional folk medicine throughout the world. Phytochemical investigations of various *Trichodesma* species have revealed that many components from this genus express significant biological and pharmacological activities. Nevertheless, there are still many *Trichodesma* species that have received very little or no attention. Further phytochemical and biological studies should be done on these plants. So, this review is an attempt to document the information on different aspects of *Trichodesma* bioactivity and highlight the need for further research and development.

Conflict of interest

The authors have declared that there is no conflict of interest.

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