A Review on Traditional Uses, Phytochemistry, and Pharmacological Activities of *Verbascum thapsus*

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Abstract

Verbascum thapsus is annual or biennial herb, which belongs to the family Scrophulariaceae. It has becomes naturalized in most temperature regions of the world, where it can be found in abundance on roadsides, meadows, and pasture lands. The plant *V. thapsus* is commonly known as "*Mullein.*" *V. thapsus* has a broad native range including Europe, North Africa, Western and Central Asia. It has been introduced to Japan, Sri Lanka, the United States of America, Australia, and New Zealand. The herb has been utilized as a medicinal herb since ancient times, and has a great potential to treat a number of ailments. Mullein is supposed to be loaded with significant number of bioactive constituents including triterpene, tetraglycosides, saponins, terpenes, flavonoids, carotenoids, tannins, carbohydrates, phenolic acid, sugars, proteins, and minerals. Due to the presence of these potent phytoconstituents, it has been traditionally used as a folk medicine for a majority of locals in different parts of world. Reported literature of the plant available from primary and secondary search engines unveil a number of pharmacological activities of the plant, including antitumor, cardiovascular, anti-inflammatory, hepatoprotective, antibacterial, antiviral, nephroprotective,

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anthelmintic, analgesic activity, etc. The aim of this chapter is to provide a comprehensive review of the various therapeutic activities of the plant along its phytochemical constituents which are responsible for its medicinal status.

Keywords

Verbascum thapsus · Mullein · Scrophulariaceae · Phytochemical moieties · Pharmacological profile

16.1 Introduction

The genus *Verbascum* L. is usually known as mullein, is a member of family Scrophulariaceae, which includes more than 400 wide-reaching species. Forty-five species (Rami-Porta et al. 2007) and a few fusions of *Verbascum* exist in the plants of Iran, 20 of which are widespread (Rechinger 1981; Sotoodeh et al. 2017). This class includes *Verbascum thapsus* L., which grows wild on flinty ground, in woodland, wasteland, clearings, and along the side of roads (Speranza et al. 2010). Plants of this type are generally utilized in tradition medicine (Gvazava and Kikoladze 2007). Its small yellow flowers are grouped solidly on a tall stem, which rolls from a large rosette of leaves. It flourishes in a wide diversity of habitats, but opt for ablaze anxious soils, where it can emerge promptly after the ground experiences light, from long-standing seeds that continue in the soil seed bank. It is a usual weedy from its large rosette of leaves. It flourishes as a wide diversity plant that proliferates by industriously producing seeds, but hardly becomes assertively insidious, because its seeds need open ground to sprout. It is a very insignificant obstacle for most agricultural crops, cause it is not a very aggressive species, being fanatical of shade from other plants and impotent to endure tilling. It also acts as a host for many insects, many of these can be dangerous to various plants. Even though those are effortless to detach by hand, populations are burdensome to abolish permanently (Watts 2000). *Verbascum* is thought to be a derivative of “barbascum,” from the Latin *barba*, meaning moustache, referring to the genus’ disheveled occurrence, while *Thapsus*, its particular name, may refer to the Greek island of the same name, where the species once flourished. The word “mullein” is derived from Middle English moleyne and Old French *moleine*, as well as the Latin *mollis*, which means “soft” and refers to the leaves (Le Strange 1977). There are 360 species of common mullein, also recognized as Wooly Mullein (*V. thapsus* L.) (Faik and Zeki 2008). *V. thapsus* L. also called as Kharghwug (Murad et al. 2011), Ghordoughkaro (Hussain et al. 2007), Gidder Tambakoo (Qureshi et al. 2007), Tamakusak (Shinwari and Gilani 2003), Khardhag (Sher et al. 2011), Jungle Tambako and Barbasco (Sher et al. 2011). Different chemical constituents have been isolated like saponins—triterpene B, triterpene A, saikogenin A (De and De Pascual 1978), thapsuine B, hydroxythapsuine, thapsuine A, hydroxythapsuine A iridoid glycosides—harpagide, verbascoside A, aucubin and isocatalpol, and their various derivatives (Bianco et al. 1984; Seifert et al. 1985b) and phenylethanoid glycosides (Warashina et al. 1991, 1992). Flavonoids have also been isolated from the plant (Souleles and Geronikaki 1989). *The Verbascum* types enclose photochemical including iridous (Arrif et al. 2008) phenylethanoids (Brownstein et al. 2017), flavonoids (Nykmukanova et al. 2019), neolignan glycosides (Akdemir et al. 2004), saponins spermine alkaloids (Halimi and Nasrabadi 2018) mucilage (Saeidi and Lorigooini 2017), vital oils, and fatty acids (Alipieva et al. 2014; Riaz et al. 2013; Boğa et al. 2016). Phenolics are another foremost group of the plants compounds that have revealed several biological results, including antibacterial and antioxidant actions against reactive oxygen species (ROS), particularly superox (Nègre-Salvayre and Salvayre 1992; Tauchen et al. 2015; Arsene et al. 2015; Carvalho et al. 2018; Rasera et al. 2019).

16.2 Historical Background of *V. thapsus*

The *Verbascum* gets its name from the Latin word "*barbascum barba*" (Jankowiak 1976), which refers to the plant's beard-like filaments (Wilhelm Jr 1974). The word *Thapsus* may have been extracted from the Isle of Siclian *Thapsos*, where mullein was collected in ancient times (Mitich 1992), or from the Tunisian island *"Thapsus*," according to legend (Jankowiak 1976). Instead of the yellow flower of the plant, *Thapsos* is a Greek term (Wilhelm Jr 1974). The plant has yellow flowers, and the Roman ladies have yellow hair. Mullein is derived from the Latin word *mollis*, which means soft (Durant 1976), and is synonymous with the modern term woolen (Mitich 1992; Notch 1989). Although the exact history of its introduction into North America is unclear, *V. thapsus* (common mullein, Scrophulariaceae) was most likely presented into North America multiple times, both inadvertently and deliberately as a remedial herb in California (Gross and Werner 1978).

By 1880, *V. thapsus* had arrived in Siskiyou county (Watson 1880), and herbarium assemblage began in the early 1900s. Not a thing is noted about the timing and specimens of its proliferation throughout the area, but it was discovered in 1934 at 1615 m in the Tahoe National Forest and has likely occupied some high-elevation locations for not less than seven decades (CalFlora Database, http://www.calflora.org). The wildflower *V. thapsus* is an alarming roadside and industrial pest (Semenza et al. 1978). However, since it is mostly found only in disturbed areas, it has not been identified as a significant toxic intruder in most parts of California (Hoshovsky 1986). *V. thapsus*, on the other hand, may form dense stands in areas with thin soils and open undergrowth, or in wooded areas after a fire. In the Owens Valley, it is said to have displaced native herbs and grasses in whole meadows.

16.3 Botany

V. thapsus is a stiff and stout herbaceous annual or biennial wild blossom. It produces a low rosette with a height of up to 61 cm. Flowers are closely packed and appear one per axil, in both male and female reproductive organs. Flowers have five sepals, five petals, a two-celled ovary, and five stamens and are yellow in color.

Fruit is a capsule that splits into two halves as it reaches adulthood. The capsule has a star-shaped facade and is ovoid in shape, measuring 3–6 mm in length. The pits are brown in color and range in length from 0.5 to 1.0 mm. In general, the basal leaves are oblong-obviate to oblanceolate entire, with small and extended petioles (10–40 cm). The leaf borders are alternately arranged and are either whole or unclearly crenate. Cauline leaves are 5–30 cm long with pinnate venation and are arranged along the stem. Mullein has an extensive taproot and a fibrous, thin secondary root system. The stem is upright and robust, with a size range of 50–180 cm. The stalk is usually plain, with leaves arranged in a row (Halvorson and Guertin 2003; Wagner et al. 1999).

16.4 Medicinal Importance of *V. thapsus*

Historically, mullein has been employed as an antidote for the respirational tract, mostly in cases of annoying coughs with bronchial blocking (Hoffmann and Manning 2002). Mullein leaves and flowers have expectorant and demulcent effects, which are employed by herbalists to cure respiratory complications for example bronchitis, dry coughs, whooping cough, tuberculosis, asthma, and harshness (Turker and Gurel 2005; Berk 1996). The flowers are gently diuretic and have a gentle and anti-inflammatory properties on the urinary area. The leaves are also diuretic, potion to reduce inflammation of the urinary system, and oppose the irritating effect of acid urine (Ambasta 1986; Turker and Camper 2002). Some herbal texts extend the remedial use to pneumonia and asthma (Turker and Gurel 2005). The leaves, roots, and the flowers are also anodyne, antibacterial, antispasmodic, astringent, emollient, nerving, vulnerary, analgesic, antihistaminic, anticancer, antioxidant, antiviral, bacteriostat, cardiodepressant, estrogenic fungicide, hypnotic, and calming (Harris 1972; Lucas 1969; Turker and Gurel 2005). The demulcent and emollient properties originate from the polysaccharide adhesive and gums that mitigate the bothered tissue. The expectorant property is the result of aspirins that stimulate fluid production. The anti-inflammatory property is due to ericoid glycosides and flavonoids that decrease tenderness (Turker and Gurel 2005). The mullein combines the expectorant exploit of its saponins with the gentle effect of its mucilage, making this a most valuable herb for the behavior of huskiness, tight coughs, bronchitis, asthma, and whooping cough (Turker and Gurel 2005). The dehydrated leaves are occasionally smoked in a common tobacco pipe to reduce the annoyance of the respiratory mucus membrane, and will totally restraint the hacking cough of utilization. The leaves are engaged with similar advantages when made into cigarettes, for asthma and irregular coughs. The flowers placed in a bottle and set in the sunshine are said to defer a fatty matter valuable as a cure for hemorrhoids. Fomentations and poultices of the leaves have been noticed helpful in hemorrhoidal complications. Mullein is said to be of much worth in diarrhea, from its amalgamation of demulcent with a strict effects and this amalgamation reinforcement of the entrails at the same time (Turker and Gurel 2005). In Europe, a sweetened infusion of flowers strained in order to separate the rough hairs is used as a domestic remedy for mild catarrhs and colic. A preserve of the flowers has also been working antagonistic to ringworm, and a purified water of the flowers was long alleged to be a treatment for erysipelas and burns (Prakash et al. 2016; Turker and Gurel 2005). A decoction of leaves was employed as a health stimulant. A decoction of roots febrifuge is used to improve toothache and also to alleviate cramps, convulsions, and migraines. The cordial of the plant and powder made from the dehydrated roots is said to rapidly separate irregular warts while massaged on them (Tyler 1994). An oil formed by macerating mullein flowers in olive oil, stored in a corked bottle during extended subjection to the sun, or by placing it near the fire for some days, is employed as a local preparation in country districts in Germany for piles and other mucus membrane inflammation, and also for frostbite and bruises. Mullein oil is prescribed for earache and discharge from the ear, and for any eczema of the external ear and its duct (Turker and Gurel 2005). Mullein oil is a beneficial demolisher of disease germs (Chopra et al. 1956; Prakash et al. 2016). The additional plants, marinated for 21 days in olive oil, are reported to make an commendable bactericide. An alcohol color is formulated by homoeopathic chemists, from the new herb with spirits of wine, which has demonstrated advantageous for migraines or sick annoyances of long status, with authority of the ear (Bianchini and Corbetta 1977; Lewis and Elvin-Lewis 2003). The seeds of mullein are reported to be toxic and should not be employed in any of these researches (Berk 1996). The seeds when thrown into the water are said to intoxicate fish, and are employed by pillagers for that motive, being a little narcotic. Major toxic rudiments disturbing the circulatory, respiratory, and central nervous systems of the fish comprise spooning, rotenone, and glycoside. The common mullein causes fish to have complexity in breathing (Wilhelm Jr 1974). The flowering stem was employed, dehydrated out by Greeks and Romans as a candle immersed in tallow for light. Mullein torches were reported to repel witches. There is authentication that at one time, it was a “magical plant” of the ancients. Agrippa, a general and priest under Caesar Augustus, reported that the aroma from the leaves had an ungovernable effect on demons. Mullein was believed to be an element in drinks and love potions, and introduced in magic spells used by witches during the Middle Ages. The women of Rome also infused the flowers and mixed the ensuing liquid with lye, using it as a clean to turn their hair golden yellow (Le Strange 1977).

16.4.1 Antitumor Activity

FO-Com (plants extracted from *V. thapsus* in pure olive oil) revealed antitumor activity. Aqueous extricate from *Densiflorum* blossom had a significant restraint result on the expansion stage of protein biosynthesis in isolated rat liver microsomes when tested for antitumor property. The saponin fraction was found to be the key culprit (Turker and Camper 2002).

16.4.2 Cardiovascular Activity

Verbacoside (1 mm) enhanced heart rate by 37%, contraction force by 9%, and coronary perfusion rate by 68% in isolated, perfuse rodent hearts (Langendorff model). As compared to the spirited α-adrenergic blocker phentolamine (1 μM), verbascoside remarkably enhanced chronotropism ($p = 0.010$), tropism ($p = 0.016$), and CPR ($p = 0.016$) (Mehrotra et al. 1989).

16.4.3 Anti-inflammatory Activity

The anti-inflammatory activity of verbascoside is possibly due to its capability to scavenge nitric oxide radicals. J774.1 cells were stimulated by seven phenylethanoids, involving acteoside (verbascoside), at concentrations of 100–200 mm compact (6.3–62.3%) nitrite assemblage in lipopolysaccharide (0.1 μg/mL). They decreased nitrite assemblage caused by lipopolysaccharide (0.1 mg/mL), interferon (100 U/mL) in mouse peritoneal evacuate macrophages by 32.2–72.4% at 200 mm. In human polymorphonuclear leukocytes, verbascoside inhibited the development of the 5-lipoxygenase product 5-HETE and leukotriene B. The critical scavenging properties of verbascoside (acteoside) were very high (Kimura et al. 1987).

16.4.4 Hepatoprotective Activity

Aucubin managed intravenously at 100 mg/kg substantially confined beagle dogs from mortal poisoning generated by digestion of *Amanita virosa* mushrooms. The action of aucubin was partially because of a defensive conclusion on the despair of m-RNA biosynthesis in the liver due to α-amanitin intoxication. It has also been revealed that aucubin confined mice from hepatic impairment produced by carbon tetrachloride intoxication (Pandey et al. 1982).

16.4.5 Antibacterial Activity

In the current study, typical plant namely *V. thapsus* has been evaluated against selected human pathogens for its antimicrobial properties. The reports showed that the plant extracts tested have important antibacterial potential in opposition to *Escherichia coli*, *Yersinia pestis*, *Pseudomonas aeruginosa*, *B. cereus*, *Listeria monocytogenes*, *and Staphylococcus aureus* (Table 16.1) (Kannan et al. 2009; Prakash et al. 2016).

Table 16.1 Taxonomic hierarchy of *Verbascum thapsus*

Taxonomic hierarchy	
Rank	Scientific name and common name
Kingdom	Plantae—plantes, Planta, Vegetal, plants
Subkingdom	Viridiplantae—green plants
Infrakingdom	Streptophyta—land plants
Superdivision	Embryophyta
Division	Tracheophyta—vascular plants, tracheophytes
Subdivision	Spermatophytina—spermatophytes, seed plants, phanérogames
Class	Magnoliopsida
Superorder	Asteranae
Order	Lamiales
Family	Scrophulariaceae—figworts, scrofulaires
Genus	*Verbascum* L.—mullein
Subspecies	*Verbascum thapsus* ssp. thapsus L; common mullein

16.4.6 Treatment of *Trichomonas vaginalis*

Acceptance of apoptosis in *Trichomonas vaginalis* due to the remove of this plant have been reported by Kashan et al. Inhibitory concentration 50% (IC50) of ethanolic abstract of *V. thapsus* and metronidazole later 24 h were 39.17 and 0.0326 μg/mL, respectively. Outcomes of this study specify that the percentage of apoptosis after behavior of parasites with various concentrations of *V. thapsus* extricate (25, 50, 100, 200, and 400 μg/mL) were 20.7, 37.04, 47.5, 62.72, and 86.35 respectively (Kashan et al. 2015).

16.4.7 Antiviral Activity

When tested for antiviral property antagonistic to Herpes simplex Virus Type-1 (HSV-1) and influenza virus A (using dye-uptake assay systems), *V. thapsus* lyophilized flower infusion showed potent anti-influenza property with IC50 < 6.25 mg/mL (Rajbhandari et al. 2009). In vitro cells, Zanon et al. discovered that an ethanolic extricate of *V. thapsus* had the greatest restraint effect antagonistic to pseudorabies virus strain RC/79 (*Herpes suis*) (2 log). The same types were reported to prevent plaque genesis induced by pseudorabies by 50% at a concentration of 35 μg/mL, 59 and 99% inhibition during the adsorption process, and virus development with the plant extract in a follow-up study (Escobar et al. 2012). Antiviral activity of *V. thapsus* against influenza virus (IC50 < 6.25 mg/mL) is also encouraging (Rajbhandari et al. 2009). Another antiviral study using methanol extracts of 100 plants in opposition to 7 viruses found 12 extricates to be effective antiviral agents at concentrating that were also noncytotoxic. In this analysis, extracts from *V. thapsus* were found to inhibit the herpes virus type-1 (Mccutcheon et al. 1995), particularly decoctions from the flowers of *V. thapsus*, which revealed very powerful effect in opposition to viruses (Mehrotra et al. 1989; Zanon et al. 1999). Although there have been no attempts to separate and estimate antiviral property of active metabolites from the ethanolic/methanolic decoctions of *V. thapsus*, a few studies on main metabolites from other plants with a high tendency to be avoided in the previous solvent decoctions have been allowed. In one study, verbascoside was observed to be most potent in opposition to respiratory syncytial virus (RSV-A2), with an EC50 of 0.80 μg/mL, an IC50 of 76.9 μg/mL, and a variability index (SI) of 85.4 (Chen et al. 1998). Aucubin, an iridoid glycoside, isolated from *Plantago asiatica* plants, was tested for antiviral property in opposition to a hepatitis B viral culture system (Hep G2 cells). While aucubin had no antiviral activity on its own, when it was preincubated with glucosidase, it showed promising results (Chang 1997).

16.4.8 Nephroprotective Activity

As compared to normal silymarin (50 mg/kg), the methanolic extract of *V. thapsus* leaves showed a nephroprotective protective effect in rats against gentamicin-induced nephrotoxicity at doses of 250 and 500 mg/kg. A drop in creatinine, urea, and urea nitrogen in the blood levels indicated a substantial reduction in nephrotoxicity. These qualities can also contribute to its ethnomedicinal status as a diuretic (Kahraman et al. 2011), so more experimental verification of active ideologies of *V. thapsus* methanolic solvent fraction is crucial.

16.4.9 Anthelmintic Activity

When concentrated in methanol, several extricate from *V. thapsus* had anthelmintic and insecticidal effects in vitro. The earthworm (*Pheretima posthuma*) was employed to measure anthelmintic behavior, with the time of paralysis and death compared to the orientation medication albendazole. *V. thapsus* extract was used at various concentrations of 5, 10, 25, 50, 75, and 100 mg, and it was found to have a significant anthelmintic effect. Leaf and fruit concentrates killed the worms in 35 and 40 min, correspondingly Leaf extricate had substantial anthelmintic property than stem extract, and root extract had the least anthelmintic commotion, according to the average paralytic and death time (Ali et al. 2012).

16.4.10 Analgesic Activity

In a mouse model of acetic acid–induced writhing and tail pressure pain, the nociceptive inhibitory properties of verbascoside were investigated. *Verbascoside* had a major analgesic effect when measured at 300 and 100 mg/kg. *Verbascoside* also had sedative properties, prolonging pentobarbital-induced anesthesia and minimizing locomotion, both of which were aided by methamphetamine (Morina et al. 2010). However, because of the sampling approach (only VB is used in these studies), the synergistic analgesic potential of all of the metabolites present in *V. thapsus* is largely unknown.

16.5 Phytochemistry

Glycoside, saponins, flavonoids, and terpenoids are the main phytoconstituents of *V. thapsus*. These phytoconstituents are partially or completely responsible for the pharmacological arrangements mentioned above. As a result, all phytoconstituents that have previously been inaccessible from *V. thapsus* are considered based on chemical categorization and the primary references of the fundamental studies mentioned.

16.5.1 Phenylethanoid Glycosides

A study of Warashina from *V. thapsus* was unable to access any phenylethanoid glycosides (H. Hussain et al. 2009). These include arenarioside, cistanoside B, alyssonoside, forsythoside B, 1′-O-β-D-(3-hydroxy-4-methoxy-phenyl)ethyl-α-L-rhamnopyranosyl-(1 → 3′)-β-D xylopyranosyl-(1 → 6′)-4′-O-feruloylglucopyranoside, 1′-O-β-D (3,4-dihydroxyphenyl)-ethyl-α-L-rhamnopyranosyl-(1 → 3′)3′- hydroxy-4′-O-β-D, glucopyranosyl-cinnamoyl-(1 → 6′) glucopyranoside,alyssonoside,1′-O-β-D-(3,4dihydroxy-phenyl)-ethyl-α-L-rhamnopyranosyl (1 → 3′)-β-D-xylopyranosyl-(1 → 6′)-4′-O-feruloylglucopyranoside, and leucosceptoside (Warashina et al. 1992). Ergosterol peroxide, docosanoic acid, oleanolic acid, and β-sitosterol were inaccessible from blossoms of *V. thapsus* (Milne and Abbott 2002).

16.5.2 Iridoid Glycosides

Verbascoside is a typical case of iridoid glycosides that were discovered much earlier than expected in the leaves of *V. thapsus* (Hattori and Shiroya 1951). The sum of aucubin, an iridoid glycoside, obtained from roots was significantly higher than segments (Seifert et al. 1985a). After segregation, an ethanolic extricate of the roots of *V. thapsus* that display anti-germination property on barley (*Hordeum vulgare*) kernels yields numerous iridoids containing harpagoside, ajugol, laterioside, and aucubin (Pardo et al. 1998). Isocatalpol, methylcatalpol (2 h), and 6-O-α-L-rhamnopyranosyl catalpol are some of the other iridoid glycosides that have been found. (Pardo et al. 1998). Warashina et al. spotted numerous iridoids from the entire herbal of V. thapsus, including 6-O-[3″-O-(3,4-dimethoxy-transcinnamoyl)] saccatoside, α-L-rhamnopyranosyl catalpol [6-O-(3′-O-p-coumaryl)-α-L-rhamnopyranosyl catalpol] (2m),6-O-(4″-O-p-coumaroyl) α-L-rhamnopyranosyl catalpol, verbascoside A, 6-O-[2″-O-(3,4-dihydroxy-trans-cinnamoyl)] α-L-rhamnopyranosyl catalpol, 6-O-[4″-O-(3,4-dihydroxy-trans-cinnamoyl)]-α-L-rhamnopyranosyl catalpol,6-O-(2″-O-(p-methoxy-trans-cinnamoyl)-α-L-rhamnopyranosyl catalpol, 6-O-(4″-O-isoferuloyl)-α-L-rhamnopyranosyl catalpol, 6-O-(2″-O-isoferuloyl)-α-L-rhamnopyranosyl catalpol, 6-O-(2″-O-feruloyl)-α-L-rhamnopyranosyl catalpol, 6-O-(3″-O-(p-methoxy-trans-cinnamoyl)-α-L-rhamnopyranosyl catalpol, 6-O-(4″-Oferuloyl)-α-L-rhamnopyranosyl catalpol and 6-O-(3″-Oisoferuloyl)-α-L-rhamnopyranosyl catalpol (Turker and Camper 2002). Another iridoid, harpagide, was isolated from *V. thapsus* inflight sections (Stavri et al. 2006). Although as from whole herbal 5-O-α-L rhamnopyranosyl (1α-3)-[α-D-glucuronopyranosyl (1α-6)]-α-D-glucopyranoside was isolated (Pardo et al. 1998). Most recently ajugol (2f), ningpogenin, 10-deoxyeucommiol, jioglutolide, 6-β-hydroxy-2-oxabicyclo[4.3.0]-Δ8–9-nonen-1one, 8-cinnamoylmyoporoside, and verbathasin A were inaccessible iridoids (Zhao et al. 2011).

16.5.3 Triterpene Tetraglycosides

Kurodo et al. recognized five triterpene tetraglycosides from the methanolic extricate of *V. thapsus* blossoms: buddlejasaponin I, ilwensisaponin A, ilwensisaponin B, ilwensisaponin C, and buddlejasaponin IA (Kuroda et al. 2012).

16.5.4 Saponins

From *V. thapsus*, different saponins which include saikogenin A, triterpene A, saikogenin B, veratric acid, α-spinasterol, thapsuine A and B (4g-h), hydroxythapsuine-A, and 3-Ofucopyranosyl saikogenin have been reported and seperated (Turker and Gurel 2005; Turker and Camper 2002; Stavri et al. 2006). These constituents may have antimicrobial, antiviral, and antitumoral activity, according to the pharmacological profile of *V. thapsus.*

16.5.5 Terpenes

Two sesquiterpenes: buddlindeterpene A and B from northern Pakistan; one diterpene, that is, from China GC-MS investigation of *V. thapsus* displayed limonene (26.57%), cineole (7.24%), caryophyllene oxide (5.91%), pinene (4.72%) 5 g, from *V. thapsus* whole plant (Hussain et al. 2009), and essential to terpenes (Dzubak et al. 2006). These multiplexes can also play a role in *V. thapsus* pharmacological movement across a wide spectrum.

16.5.6 Flavonoids and Carotenoids

Flavonoids have the ability to counteract the effects of reactive free radicals, and as a result, they have a high standing in antioxidant, cancer, diabetes, and a diversity of other diseases associated to oxidative stress (Nijveldt et al. 2001). The leaf total phenolic content was 0.124 mg/g dry weight, stem 0.166 mg/g dry weight, and root total flavonoid content was 0.024 mg/g dry weight (Kogje et al. 2010). The configuration of flavonoids was investigated in the roots and aerial sections of plants, which are stems, leaves, blossoms, and seeds, from 22 *Verbascum* species (Kalinina et al. 2014). Seven flavonoids from *V. thapsus* were inaccessible: acacetin-7-O-D-glucoside, luteolin, cynaroside, kaempferol, quercetin, and rutin. A new flavonoid, apigetrin, has been discovered in a 70% aqueous acetone inflight concentrate (Zhao et al. 2011). Separation and classification of another new flavonoid, 4′7-dihydroxyflavone-4′-rhamnoside, as well as 6-hydroxyluteolin-7-glucoside and 3-′-methylquercetin, from the leaves and flowers of *V. thapsus* has also been identified (Souleles and Geronikaki 1989). Carotenoids, especially zeaxanthin, have been extracted from the seed oil of *V. thapsus* and may be used as dietary sources. Another research discovered that *V. thapsus* seed oils have relatively greater α-tocopherol levels, with a ratio of 1:10 for α- to γ-isomers (Jia et al. 2009).

16.5.7 Carbohydrates

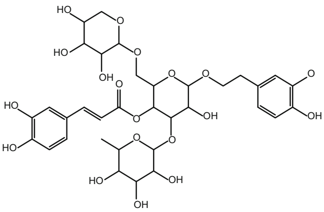
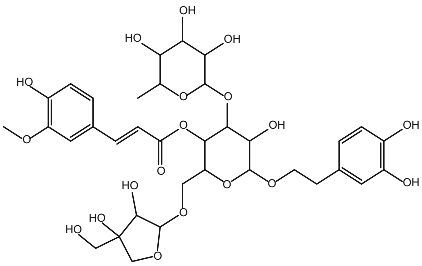
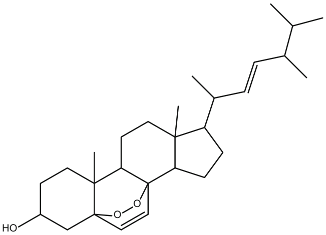
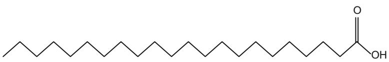
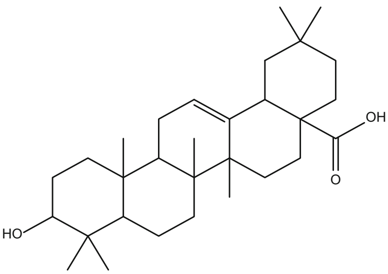
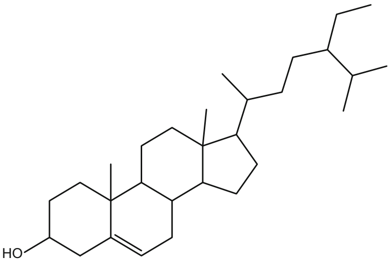
Verbascose, sucrose, hepatose, octaose, and nonaose are some of the carbohydrates isolated from *V. thapsus* (Turker and Gurel 2005; Hattori and Hatanaka 1958).

Some examples of constructions can be found in Table 16.2.

16.6 Toxicity Studies

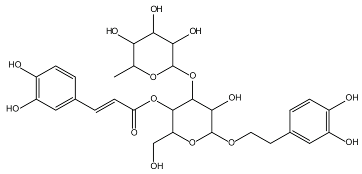
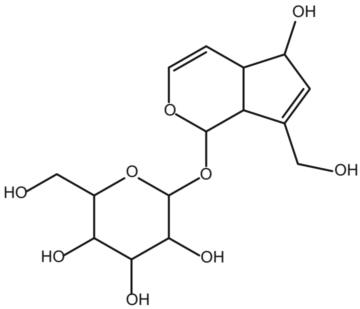
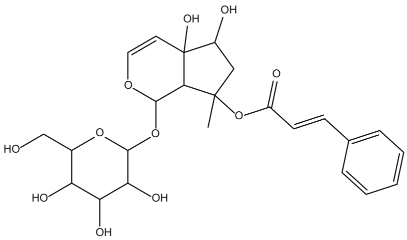
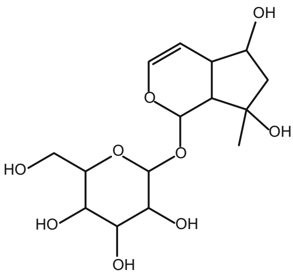
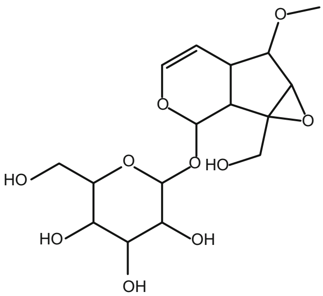
There is no details on the mullein flower’s genotoxicity, carcinogenicity, reproductive, or developmental effects. The operation and toxicity of certain *V. nigrum* extricates and decoctions were investigated. The extracts of *V. nigrum* had a low toxicity profile. During the 72-h period following the supervision of doses up to 5000 mg/kg, no effect on mouse behavioral responses, and no cases of transience were noticed (Kalinina et al. 2014). A radish kernel and brine shrimp bioassay were used to assess the toxicity of various *V. thapsus* abstracts. At the higher doses of 1000 mg/dL, all of the extracts (water, methanol, and ethanol) were found to be healthy. Surprisingly, aqueous extract decoction was more toxic than distillation, suggesting that it may involve increased toxic complexes than other forms of extricates. A case study on the effects of a herbal drug amalgamation called CKLS (colon, kidney, liver, spleen) that contains *V. thapsus* as one of the main ingredients is very interesting. The patient developed severe kidney damage after a 5-day course of CKLS. Despite the fact that CKLS contains 10 other plant mixtures, further

Table 16.2 Structures of active constituents of *Verbascum thapsus*

Active constituents	Structure	References
Arenarioside		Milne and Abbott (2002)
Alyssonoside		Milne and Abbott (2002)
Ergosterol peroxide		Milne and Abbott (2002)
Docosanoic acid		Milne and Abbott (2002)
Oleanolic acid		Milne and Abbott (2002)
B-sitosterol		Milne and Abbott (2002)

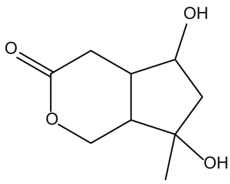
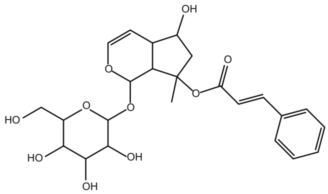
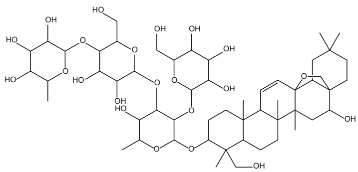
(continued)

Table 16.2 (continued)

Active constituents	Structure	References
Verbascoside		Zhao et al. (2011)
Aubucin		Zhao et al. (2011)
Harpagoside		Zhao et al. (2011)
Ajugol		Zhao et al. (2011)
Methylcatalpol		Zhao et al. (2011)

(continued)

Table 16.2 (continued)

Active constituents	Structure	References
Jioglutolide		Zhao et al. (2011)
8-Cinnamoylmyoporoside		Zhao et al. (2011)
Buddlejasoponin		Kuroda et al. (2012)

research is needed to rule out *V. thapsus* as a cause of nephrotoxicity, particularly because herbal drugs are frequently dismissed.

16.7 Conclusion

The multiple benefits of *V. thapsus* made it a true miracle of nature. It significantly possesses a variety of secondary metabolites, thus representing useful sources of bioactive compounds and preparation with healthy encouraging effects such as anti-inflammatory, hepatoprotective, nephroprotective, cardiovascular, antitumor, etc. The diverse effects of mullein are attributed to the presence of various triterpene, fatty acids, and phytosterols. The pharmacological investigation confirmed the empirical traditional application of mullein in humans for the treatment of digestive disorders, tumor formation, urinary tract infection, and certain skin diseases. Mullein evaluated for phytochemical constituents had great potential to act as a source of useful lead molecules and ameliorate health condition of consumers due to the presence of various bioactive compounds that are indispensable for good health.

References

Akdemir ZŞ, Tatli II, Bedir E, Khan IA (2004) Neolignan and phenylethanoid glycosides from verbascum salviifolium boiss. Turk J Chem 28(5):621–628

Ali N, Shah SWA, Shah I, Ahmed G, Ghias M, Khan I, Ali W (2012) Anthelmintic and relaxant activities of Verbascum thapsus mullein. BMC Complement Altern Med 12(1):29

Alipieva KI, Orhan IE, Cankaya IIT, Kostadinova EP, Georgiev MI (2014) Treasure from garden: chemical profiling, pharmacology and biotechnology of mulleins. Phytochem Rev 13 (2):417–444

Ambasta SS (1986) The useful plants of India. Publications & Information Directorate CSIR, New Delhi

Arrif S, Lavaud C, Benkhaled M (2008) Iridoids from verbascum dentifolium. Biochem Syst Ecol 8 (36):669–673

Arsene AL, Rodino S, Butu A, Petrache P, Iordache O, Butu M (2015) Study on antimicrobial and antioxidant activity and phenolic content of ethanolic extract of Humulus Lupulus. Farmacia 63 (6):851–857

Berk SA (1996) The naturalist's herb guide. Black Dog & Leventhal Pub. https://doi.org/10.1002/ptr.1653REVIEW

Bianchini F, Corbetta F (1977) Health plants of the world atlas of medicinal plants (No. C/ 581.63402 B5)

Bianco A, Guiso M, Passacantilli P, Francesconi A (1984) Iridoid and phenypropanoid glycosides from new sources. J Nat Prod 47(5):901–902

Boğa M, Ertaş A, Haşimi N, Demirci S, Yılmaz MA, Temel H, Kolak U (2016) Phenolic profile, fatty acid and essential oil composition analysis and antioxidant, anti-Alzheimer and antibacterial activities of verbascum flavidum extracts. Chiang Mai J Sci 43(5):1090–1101

Brownstein KJ, Gargouri M, Folk WR, Gang DR (2017) Iridoid and phenylethanoid/ phenylpropanoid metabolite profiles of scrophularia and verbascum species used medicinally in North America. Metabolomics 13(11):133

Carvalho R, Carollo C, De Magalhães J, Palumbo J, Boaretto A, Nunes e Sá I et al (2018) Antibacterial and antifungal activities of phenolic compound-enriched ethyl acetate fraction from cochlospermum regium (Mart. Et. Schr.) pilger roots: mechanisms of action and synergism with tannin and gallic acid. S Afr J Bot 114:181–187

Chang IM (1997) Antiviral activity of aucubin against hepatitis B virus replication. Phytother Res 11(3):189–192

Chen JL, Blanc P, Stoddart CA, Bogan M, Rozhon EJ, Parkinson N et al (1998) New iridoids from the medicinal plant Barleria prionitis with potent activity against respiratory syncytial virus. J Nat Prod 61(10):1295–1297

Chopra RN, Nayar SL, Chopra IC (1956) Glossary of Indian medicinal plants, vol 1. Council of Scientific & Industrial Research, New Delhi

De P, De Pascual TJ (1978) Componentes del verbascum thapsus L. II. Aceite De Las Senrillas

Durant MB (1976). Who named the daisy? Who named the rose? Dodd & Mead Company, New York

Dzubak P, Hajduch M, Vydra D, Hustova A, Kvasnica M, Biedermann D et al (2006) Pharmacological activities of natural triterpenoids and their therapeutic implications. Nat Prod Rep 23 (3):394–411

Escobar FM, Sabini MC, Zanon SM, Tonn CE, Sabini LI (2012) Antiviral effect and mode of action of methanolic extract of Verbascum thapsus L. on pseudorabies virus (Strain Rc/79). Nat Prod Res 26(17):1621–1625

Faik A, Zeki A (2008) Revision of the genus Verbascum L.(Group A) in Turkey. Bot Res J 1 (1):9–32

Gross KL, Werner PA (1978) The biology of Canadian weeds.: 28. Verbascum thapsus L. and V. blattaria L. Can J Plant Sci 58(2):401–413

Gvazava L, Kikoladze V (2007) Verbascoside from Verbascum phlomoides. Chem Nat Compd 43 (6):710–711

Halimi M, Nasrabadi M (2018) Isolation and identification macrocyclic spermine alkaloid (protoverbine) from Verbascum speciosum. Quart J Iran Chem Commun 6(2, pp. 109–217, Serial No. 19), 143–147

Halvorson W, Guertin P (2003) Factsheet for: Verbascum thapsus L. University of Arizona Biological Sciences East Tucson, Arizona

Harris BC (1972) The compleat herbal

Hattori S, Hatanaka S (1958) Oligosaccharides in Verbascum thapsus L. Bot Mag (Tokyo) 71 (845–846):417–424

Hattori S, Shiroya T (1951) The sugars in the seeds and seedlings of Pinus thunbergii. Arch Biochem Biophys 34(1):121–134

Hoffmann FW, Manning M (2002) Herbal medicine and botanical medical fads. Psychology Press. https://doi.org/10.1002/ptr.1653REVIEW

Hoshovsky M (1986) Element Stewardship abstract for Verbascum thapsus, common mullein. The Nature Conservancy, Arlington

Hussain H, Aziz S, Miana GA, Ahmad VU, Anwar S, Ahmed I (2009) Minor chemical constituents of Verbascum thapsus. Biochem Syst Ecol 37(2):124–126

Hussain F, Shah SM, Sher H (2007) Traditional resource evaluation of some plants of Mastuj, District Chitral, Pakistan. Pak J Bot 39(2):339–354

Jankinowiak J (1976) Bring mullein back from the weedy wilds. Org Gard Farming 23(7):63–65

Jia C, Shi H, Jin W, Zhang K, Jiang Y, Zhao M, Tu P (2009) Metabolism of echinacoside, a good antioxidant, in rats: isolation and identification of its biliary metabolites. Drug Metab Dispos 37 (2):431–438

Kahraman C, Ekizoglu M, Kart D, Akdemir Z, Tatli II (2011) Antimicrobial activity of some verbascum species growing in Turkey. Fabad J Pharm Sci 36:11–15

Kalinina SA, Elkina OV, Kalinin DV, Syropyatov BY, Dolzhenko AV (2014) Diuretic activity and toxicity of some Verbascum nigrum extracts and fractions. Pharm Biol 52(2):191–198

Kannan P, Ramadevi S, Hopper W (2009) Antibacterial activity of Terminalia chebula fruit extract. Afr J Microbiol Res 3(4):180–184

Kashan ZF, Arbabi M, Delavari M, Hooshyar H, Taghizadeh M, Joneydy Z (2015) Effect of Verbascum thapsus ethanol extract on induction of apoptosis in trichomonas vaginalis in vitro. Infect Disord Drug Target 15(2):125–130

Kimura S, Favel A, Steinmetz M, Regli P, Olivier E, Elias R, Balansard G (1987) In vitro antiinflammatory activity of triterpenoid saponins. Planta Med 60:50–53

Kogje K, Jagdale V, Dudhe S, Phanikumar G, Badere R (2010) Antioxidant property and phenolic compounds of few important plants from trans-Himalayan regions of North India. J Herb Med Toxicol 4(2):145–151

Kuroda M, Iwabuchi K, Mimaki Y (2012) Triterpene tetraglycosides from the flowers of Verbascum thapsus. 生薬學雜誌. Shoyakugaku Zasshi 66(2):91–92

Le Strange R (1977) History of herbal plants. Angus & Robertson, London

Lewis WH, Elvin-Lewis MP (2003) Medical botany: plants affecting human health. Wiley, New York

Lucas RM (1969) Common and uncommon uses of herbs for healthful living

Mccutcheon A, Roberts T, Gibbons E, Ellis S, Babiuk L, Hancock R, Towers G (1995) Antiviral screening of British Columbian medicinal plants. J Ethnopharmacol 49(2):101–110

Mehrotra R, Ahmed B, Vishwakarma R, Thakur R (1989) Verbacoside: a new luteolin glycoside From Verbascum thapsus. J Nat Prod 52(3):640–643

Milne RI, Abbott RJ (2002) The origin and evolution of tertiary relict floras. Adv Bot Res 38:281–314

Mitich LW (1992) Tansy. Weed Technol 6(1):242–244

Morina F, Jovanovic L, Mojovic M, Vidovic M, Pankovic D, Veljovic Jovanovic S (2010) Zinc-induced oxidative stress in Verbascum thapsus is caused by an accumulation of reactive oxygen species and quinhydrone in the cell wall. Physiol Plant 140(3):209–224

Murad W, Ahmad A, Gilani SA, Khan MA (2011) Indigenous knowledge and folk use of medicinal plants by the tribal communities of Hazar Nao Forest, Malakand District, North Pakistan. J Med Plant Res 5(7):1072–1086

Nègre-Salvayre A, Salvayre R (1992) Quercetin prevents the cytotoxicity of oxidized LDL on lymphoid cell lines. Free Radic Biol Med 12(2):101–106

Nijveldt RJ, Van Nood E, Van Hoorn DE, Boelens PG, Van Norren K, Van Leeuwen PA (2001) Flavonoids: a review of probable mechanisms of action and potential applications. Am J Clin Nutr 74(4):418–425

Notch LW (1989) Common mullein—the roadside Torch Parade. Weed Technol 3(4):704–705

Nykmukanova M, Mukazhanova ZB, Kabdysalym K, Eskalieva B, Beyatli A (2019) Flavonoids from verbascum marschallianum and V. orientale. Chem Nat Compd 55(5):937–938

Pandey D, Tripathi N, Tripathi R, Dixit S (1982) Fungitoxic and phytotoxic properties of the essential oil of Hyptis suaveolens/Fungitoxische und phytotoxische eigenschaften des ätherischen öis von hyptis suaveolens. Zeitsch Pflanzenkrankh Pflanzensch/J Plant Dis Prot:344–349

Pardo F, Perich F, Torres R, Delle Monache F (1998) Phytotoxic iridoid glucosides from the roots of Verbascum thapsus. J Chem Ecol 24(4):645–653

Prakash V, Rana S, Sagar A (2016) Studies on antibacterial activity of Verbascum thapsus. J Med Plant Stud 4(3):101–103

Qureshi RA, Ahmed M, Ghufran MA, Bashir BH (2007) Indigenous knowledge of some important wild plants as a folk medicines in the area of Chhachh (Distt. Attock) Punjab, Pakistan. Pak J Bot 39(7):2291–2299

Rajbhandari M, Mentel R, Jha P, Chaudhary R, Bhattarai S, Gewali M, et al (2009) Antiviral activity of some plants used in Nepalese traditional medicine. Evid-Based Complem Alternat Med 6(4):517–522

Rami-Porta R, Ball D, Crowley J, Giroux DJ, Jett J, Travis WD et al (2007) The Iaslc Lung Cancer Staging Project: proposals for the revision of the T descriptors in the forthcoming (seventh) edition of the Tnm classification for lung cancer. J Thorac Oncol 2(7):593–602

Rasera GB, Hilkner MH, De Alencar SM, De Castro RJS (2019) Biologically active compounds from white and black mustard grains: an optimization study for recovery and identification of phenolic antioxidants. Ind Crop Prod 135:294–300

Rechinger K (1981) Flora Iranica, Scrophulariaceae I, Akademische Druck-U. Verlagsanstalt, Graz, p 134

Riaz M, Zia-Ul-Haq M, Jaafar HZ (2013) Common mullein, pharmacological and chemical aspects. Rev Bras 23(6):948–959

Saeidi K, Lorigooini Z (2017) Determination of mucilage content of mullein (Verbascum songaricum) populations. J Pharm Sci Res 9(12):2641–2643

Seifert K, Schmidt J, Lien N, Johne S (1985a) Iridoide Aus Verbascum-Arten. Planta Med 51 (05):409–411

Seifert K, Schmidt J, Lien N, Johne S (1985b) Iridoids from Verbascum species. Planta Med 51 (5):409–411

Semenza R, Young J, Evans R (1978) Influence of light and temperature on the germination and seedbed ecology of common mullein (Verbascum thapsus). Weed Sci 21(6):577–581

Sher Z, Khan Z, Hussain F (2011) Ethnobotanical studies of some plants of Chagharzai Valley, District Buner, Pakistan. Pak J Bot 43(3):1445–1452

Shinwari ZK, Gilani SS (2003) Sustainable harvest of medicinal plants at Bulashbar Nullah, Astore (Northern Pakistan). J Ethnopharmacol 84(2–3):289–298

Sotoodeh A, Attar F, Civeyrel L (2017) Verbascum songaricum subsp. subdecurrens: a new record, typification and the true identity of V. aspinum as a new synonym of V. stachydiforme in the flora of Iran. Kew Bull 72(2):24

Souleles C, Geronikaki A (1989) Flavonoids from Verbascum thapsus. Sci Pharm 57(1):59–61
Speranza L, Franceschelli S, Pesce M, Reale M, Menghini L, Vinciguerra I et al (2010) Antiinflammatory effects in Thp-1 cells treated with verbascoside. Phytother Res 24 (9):1398–1404
Stavri M, Mathew K, Gibbons S (2006) Antimicrobial constituents of scrophularia deserti. Phytochemistry 67(14):1530–1533
Tauchen J, Doskocil I, Caffi C, Lulekal E, Marsik P, Havlik J et al (2015) In vitro antioxidant and anti-proliferative activity of ethiopian medicinal plant extracts. Ind Crop Prod 74:671–679
Turker AU, Camper N (2002) Biological activity of common mullein, a medicinal plant. J Ethnopharmacol 82(2–3):117–125
Turker AU, Gurel E (2005) Common mullein (Verbascum thapsus L.): recent advances in research. Phytother Res 19(9):733–739
Tyler VE (1994) Herbs of choice: the therapeutic use of phytomedicinals. Pharmaceutical Products Press (Imprint of Haworth Press, Inc.), Binghamton
Wagner WL, Herbst DR, Sohmer SH (1999) Manual of the flowering plants of Hawai‘i. University of Hawai’i Press
Warashina T, Miyase T, Ueno A (1991) Iridoid glycosides from Verbascum thapsus L. Chem Pharm Bull 39(12):3261–3264
Warashina T, Miyase T, Ueno A (1992) Phenylethanoid and lignan glycosides from Verbascum thapsus. Phytochemistry 31(3):961–965
Watson S (1880) Geological survey of California, Botany, vol II. Welch, Bigelow And Company: University Press, Cambridge, MA
Watts D (2000) Elsevier’s Dictionary of plant names and their origin. Elsevier Science BV
Wilhelm G Jr (1974) The mullein: plant piscicide of the mountain folk culture. Geogr Rev 64 (2):235–252
Zanon SM, Ceriatti FS, Rovera M, Sabini LJ, Ramos BA (1999) Search for antiviral activity of certain medicinal plants from Cordoba, Argentina. Rev Latinoamericana Microbiol-Mexico 41 (2):59–62
Zhao Y-L, Wang S-F, Li Y, He Q-X, Liu K-C, Yang Y-P, Li X-L (2011) Isolation of chemical constituents from the aerial parts of Verbascum thapsus and their antiangiogenic and antiproliferative activities. Arch Pharm Res 34(5):703–707