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REVIEW ARTICLE

TOXIC ALCOHOLS: ALIPHATIC UNSATURATED ALCOHOLS

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Summary

Short-chain unsaturated aliphatic alcohols exist as volatile liquids, some of them are used in both industrial and non-industrial environments, and some of them are natural products of different organisms. These alcohols very often work as semiochemicals, including acting as pheromones, attractants, repellents, etc.. Long-chain poly-unsaturated alcohols are often toxic principals of certain plants, thereby presenting a risk to humans.

Key words: unsaturated alcohols; alkenols; alkynols; semiochemicals; plant toxins; cicutoxin; oenanthotoxin

INTRODUCTION

This article focuses on aliphatic unsaturated alcohols – their properties and uses. The aliphatic unsaturated alcohols can be regarded as derivatives of alkenes in which hydroxyl groups have replaced one or more hydrogen atoms. From the toxicological point of view short-chain unsaturated aliphatic alcohols are less relevant than saturated alcohols (Patočka and Kuča, 2012), while long-chain poly-unsaturated alcohols are often toxic principals of certain organisms. Alcohols with one double bond (monounsaturated) are important representatives of chemical industry. Some of them are also present in natural sources, for example, in plants as fragrant substances. Some short-chain unsaturated alcohols are components of mushroom flavor, such as 1-octen-3-ol or 2-octen-1-ol (Zawirska-Wojtasiak *et al*., 2004). Some of these alcohols have insect pheromone activity (Larue and Barbier, 1976; Vanhaelen *et al.*, 1978; Robert *et al*., 2004). Although any alcohol can be considered as toxic, the term *toxic alcohol* has traditionally referred to methanol, isopropanol, and ethylene glycol (McMahon *et al*., 2009). Nevertheless, some natural unsaturated alcohols pose risks as well being considered as toxicologically important compounds, such as cicutoxin from the water hemlock (*Cicuta maculata*) (Schep et al., 2009). The criterion for inclusion of unsaturated aliphatic alcohol to this review was chemical structure and available

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information about its toxicity. A few longer chain unsaturated alcohols are derived from natural sources, which are often significant reservoirs of biologically active substances and provide new insights into their biological activity (Molaison *et al*., 1959). They were selected substances with proven additional biological activity. Another criterion of a biological property of the substance was an allergic reaction, ability to irritate the skin or mucous membranes, their antibacterial activity and so on. Some important industrially used unsaturated alcohols, as well as some natural unsaturated alcohols are of interest to this review article.

PHYSICO-CHEMICAL PROPERTIES OF UNSATURATED ALIPHATIC ALCOHOLS

Unsaturated aliphatic alcohols contain a hydrocarbon fragment derived from an unsaturated fatty, non-aromatic hydrocarbon. The chemical properties of any given unsaturated aliphatic alcohol depend on the nature of the alkyl group, on the number of double and triple bonds and on their position in carbon chain. The hydroxyl group generally makes the alcohol molecule polar and can form hydrogen bonds with other hydroxyl groups and hydrogen bonding groups in other molecules. This hydrogen bonding means that alcohols can be used as protic solvents. These alcohols exist as volatile liquids at ambient temperatures and have varying solubility in water, with the longer chain alcohols being less soluble.

ALCOHOLS WITH ONE DOUBLE BOND

Short-chain alcohols (Two to six carbon chains)

Two carbon chain

Ethenol or vinyl alcohol (CH_2=CH-OH) (CAS 557-75-5) is the simplest unsaturated aliphatic alcohol. It is an unstable compound that converts under normal conditions (tautomerizes) to acetaldehyde. Vinyl alcohol is a significant raw material in the manufacture of polyvinyl alcohol, an important water-soluble polymer with a wide range of uses. Vinyl alcohol is much more toxic than ethanol. Its LD_{50} in rat at oral administration is 64 mg/kg (Cohen *et al*., 1974). The LD_{50} of ethanol at the same conditions is 7 060 mg/kg (Wiberg *et al*., 1970). Accidental poisoning of human has not yet been reported.

Three carbon chain

2-propen-1-ol (allyl alcohol, CH_2=CH-CH_2-OH, CAS 107-18-6) is an important raw material of synthetic chemistry, which is used for the preparation of pharmaceuticals, plasticizers and other important compounds. A number of toxicity studies of allyl alcohol have been reported. These studies were performed in different animal species, such as rats, mice, rabbits, dogs, and frogs by a number of various exposures including inhalation, ingestion, parenteral, and subcutaneous administration. Acute inhalation toxicity was studied in rats exposed for 1 hour (0, 50, 200, or 400 ppm), 4 hours (0, 20, 50, or 100 ppm), or 8 hours (0, 10, 20, or 50 ppm) to allyl alcohol. Mortality was limited to 1 male exposed for 8 hours to 50 ppm. Clinical findings of gasping, rales, increased respiration noted at higher exposure levels were rapidly reversed. Mild nasal inflammation was found at the lowest exposure levels (50 ppm/1 hour, 20 ppm/4 hour, and 10 ppm/8 hour). These effects were considered reversible and were not associated to related clinical signs. Severe, irreversible nasal olfactory epithelial lesions were present in 50 ppm/8-hour males. The nasal olfactory epithelial lesions (NOEL) for irreversible effects were observed in 400 ppm/1-hour, 10 ppm/4-hour, and 20 ppm/8-hour (Li *et al*., 2012). In contrast, the OECD SIDS for UNEP lists the NOAEL (no adverse observable effect limit) for inhalation toxicity in male rats as 12 mg/m^3 (5 ppm) based on a significant decrease in body weight gain in groups exposed to 47 mg/m^3 (20 ppm) and higher. (2005 - http://www.inchem.org/documents/sids/sids/107186.pdf)

Allyl alcohol induced hepatotoxicity in rats (Joglekar and Balwani, 1967). Hepatotoxicity of allyl alcohol involves its oxidation to products including acrolein and subsequent protein sulfhydryl loss and lipid peroxidation (Maddox *et al.*, 2003). Oxidation of allyl alcohol is mediated by liver alcohol dehydrogenase (Belinsky *et al*., 1985).

The OECD SIDS report for UNEP includes a determination of kidney damage in rats ingesting allyl alcohol in drinking water. In a repeated dose oral toxicity study, 2-propen-1-ol had adverse effects on kidney tissues in rats, administered in the drinking water continuously for 15 weeks at or above a level of 100 ppm (8.3 mg/kg bw/day in males and 6.9 mg/kg bw/day in females). The NOAEL was 50 ppm for 2-propen-1-ol in drinking water (equivalent to 4.8 mg/kg bw/day in male rats and 6.2 mg/kg bw/day in female rats) based on adverse effects on kidney tissues (increases in absolute kidney weight and relative kidney

weight) for females and on an increase in relative stomach weight for male and females at 100 ppm. The studies used resulted in a NOAEL of 50 ppm of allyl alcohol (male rats) and was also used to determine the Reference dose of $5x10^{-3}$ mg/kg/day for the US EPA drinking water standards.

Four carbon chain

Butenols. There are six isomers of butenol, ***1-buten-1-ol*** (CAS 57323-59-8), ***2-buten-1-ol*** (CH_3-CH=CH-CH_2-OH) (CAS 6117-91-5) and ***3-buten-1-ol*** (CAS 627-27-0) and their cis and *trans* isomers. Out of these, 2-buten-1-ol, also called ***crotyl alcohol*** or ***crotonyl alcohol***, is the most important. It is a clear liquid that is moderately soluble in water, and miscible with the majority of organic solvents. Acute toxicity of crotyl alcohol is characterised by LD_{50} value of 793 mg/kg in rat at oral administration, 1084 mg/kg in rabbit at skin application and LCLo value of 2000 ppm/4 hours in rat at inhalation (Smyth *et al*., 1962). Virtually nontoxic crotyl alcohol can be oxidized in the liver to the toxic un-saturated aldehyde, crotonaldehyde (CAS 123-73-9) (Fontaine *et al*., 2002). Recent confirmation that the toxic crotonaldehyde contributes to protein damage during lipid peroxidation confers interest on the molecular actions of this substance.

An important derivative of crotonyl alcohol is its 3-phenyl derivative, a substance of natural origin known as ***cinnamyl alcohol*** (3-phenyl-2-propen-1-ol) (CAS 104-54-1). Its acute toxicity is characterised by LD_{50} value of 2000 mg/kg in rat, 2675 mg/kg in mouse, and 2675 mg/kg in guinea pig after oral administration and more than 5000 mg/kg in rabbit at skin application (Anonymous, 1974).

The indivividual toxic properties of longer chain alcohols are not well known, and also from a toxicological point of view do not represent a significant health risk. As the chain lengths increase, more alcohols are found in natural products of plants and often play a role in messaging, such as attractants or in fragrances. For example, unsaturated alcohols 1-octen-3-ol (CAS 3391-86-4) and 2-octen-1-ol (CAS 22104-78-5) are components of mushroom flavor (Wnuk *et al*., 1983). 1-octen-3-ol has been also identified as the most potent stimulant in cattle odour to attract tsetse *Glossina pallidipes* and *G. morsitans morsitans* (Hall *et al*., 1984). Furthermore, it is present in human breath and sweat and may attract mosquitos.

Long-chain alcohols (eighteen and longer carbon chains)

Higher fatty acohols with one double bond (Fig. 1) could be found in nature, such as cis-6-octadecen-1-ol (***petroselinyl alcohol***) (CAS 2774-87-0), cis-9-octadecen-1-ol (***oleyl alcohol***) (CAS 143-28-2) and cis-11-octadecen-1-ol (vaccenyl alcohol) (CAS 62972-93-4). Some of these alcohols have insect pheromone activity, and generally are not very toxic. As an example, 11-eicosen-1-ol (CAS 68760-58-7) is a major component of the alarm pheromone secreted by the sting apparatus of the worker honeybee (Brodmann *et al*., 2009). Cis-11-docosen-1-ol (CAS 629-98-1) is present in marine ctenophores, together with some wax esters (Graeve *et al*., 2008).

Gyptol, an acetoxy derivative of a 16-carbon alcohol with one double bond (10-acetoxy *cis*-7-hexadecen-1-ol), was described as a strong attractive substance secreted by a female moth (*Porthetria dispar*) (Butenandt *et al*., 1959). Also other higher unsaturated alcohols have pheromone activity, as, for instance, *cis*-7-dodecen-1-ol (CAS 20056-92-2) from Cabbage looper (*Trichoplusia ni*) (Berger, 1966), *cis*-9-tetradecen-1-ol (CAS 35153-15-2) from fall army worm (*Lyphygma frugiperda*) (Sekul and Sparks, 1967), and others.

Avocadene (16-heptadecene-1,2,4-triol) (CAS 24607-08-7), a fatty triol with one double bond, isolated from avocado fruit (*Persea americana*) has been tested for its anti-bacterial and anti-inflammatory properties (Lu *et al*., 2012).

Citronellol (3,7-dimethyl-6-octen-1-ol) (CAS 106-22-9) is a natural monoterpenoid used in perfumes and insect repellents (Tailor and Schreck, 1985). It was reported that citronellol exhibits antinociceptive and anti-inflammatory activities (Brito *et al*., 2012) and is also relevant for its nematicidal activity (Abdel-Rahman *et al.*, 2013). Acute toxicity of citronellol to mammals is low. The LD_{50} in mouse is 4000 mg/kg after intramuscular and 880 mg/kg after subcutaneous administration and LD_{50} in rat is 3450 mg/kg at oral application (Anonymous, 1975).

Bruchins are mono- and bis 3-(hydroxypropanoyl) esters of long chain unsaturated diols. Bruchin A and bruchin B have been isolated and identified from two genera of the family *Bruchidae*, and have been shown to be responsible for the mi-

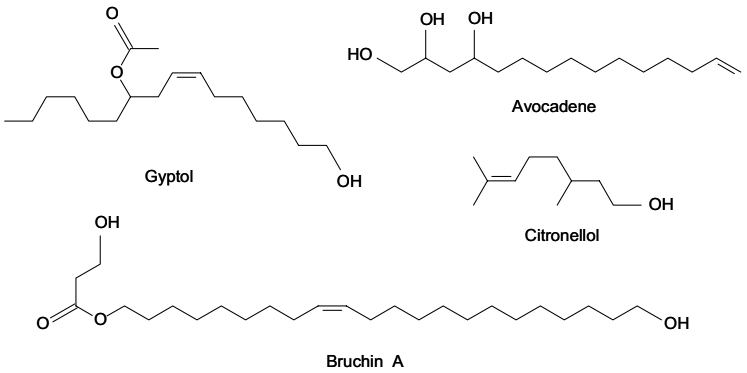

Fig. 1. Some higher fatty acohols with one double bond

togenic activity observed on pea pods resulting from oviposition by the pea weevil, *Bruchus pisorum* (Olivera *et al*., 2000).

ALCOHOLS WITH TWO OR MORE DOUBLE BONDS

Higher fatty acohols with two or more double bonds (Fig. 2) could be found in nature mainly as pheromones and other semiochemicals. One of the first isolated pheromones was ***bombykol***, (10E,12Z)-hexadecen-1-ol (CAS 765-17-3) from gypsy moth (*Porthetria dispar*) (Butenandt *et al*., 1959). Among other pheromones of this group belong, for example, 2-methyl-6-methylene-7-octen-4-ol and 2-methyl-6-methylene-2,7-octadien-4-ol (CAS 35628-00-3) from bark beetle (*Ips confusus*) (Vite *et al*., 1963) or ***codlemone*** (8,10-dodecadienol) (CAS 57002-06-9) which is secreted by the codling moth *Cydia pomonella* (Beroza *et al*., 1974).

Geraniol ((E)-3,7-dimethyl-2,6-octadien-1-ol) (CAS 106-24-1) is a monoterpenoid alcohol, a powerful ingredient extracted from geranium oil and some other natural oils. It is effective in repelling a wide variety of insects, including mosquitoes, houseflies, stable flies, horn flies, cockroaches, fire ants, fleas, gnats, dog ficka and others (Pohlit *et al*., 2011). From a biological point of view geraniol is a very active compound. It significantly reduces lipid peroxidation by-products and improves the status of enzymatic and non-enzymatic antioxidants as well as modulates the status of phase I and phase II detoxification enzymes, favoring the excretion of carcinogenic metabolite, during DMBA-induced oral carcinogenesis (Vinothkumar and Manoharan, 2011). The toxicity of geraniol to mammals is low. The LD_{50} in mouse is 4000 mg/kg after intramuscular and 1090 mg/kg after subcutaneous administration and LD_{50} in rat is 3600 mg/kg at oral application (Yamawakit, 1962).

Nerol ((Z)-3,7-dimethyl-2,6-octadien-1-ol) (CAS 106-25-2), a monoterpene found in many essential oils such as lemongrass and hops, is an isomer of geraniol.

Linalool (3,7-dimethyl-1,6-octadien-3-ol) (CAS 78-70-6) is a component of many essential oils, including orange, lavender, rose, rosewood, and coriander oils. The toxicity of linalool to mammals is low. The LD_{50} values in most laboratory animals (rats, mice and rabbits) and different routes of administration (oral, intramuscular, skin and subcutaneous) vary, but are about 3 g/kg (Marhold, 1986). The main drawback of linalool is the risk of skin irritation and initiation of allergic reactions. Linalool in its pure form is not a skin allergen. However, after its oxidation it can cause allergic reactions/sensitivity at high concentrations (Bråred Christensson *et al*., 2009). Pure linalool has anti-cancer effect (Loizzo *et al*., 2008) and its use in clinical practice is intensively studied (Ravizza *et al*., 2008). Linalool also appears as a hope in leukemia therapy, as, among the substances tested, linalool showed the strongest activity against histiocytic lymphoma cells U937 and Burkitt lymphoma cells P3HR1 (Chiang *et al*., 2003).

Farnesol ((*2E,6E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol) (CAS 4602-84-0) is a natural acyclic sesquiterpene alcohol which is present in many essential oils. It is insoluble in water, but miscible with oils. It is the building block of most, and possibly all, acyclic sesquiterpenoids and is an im-

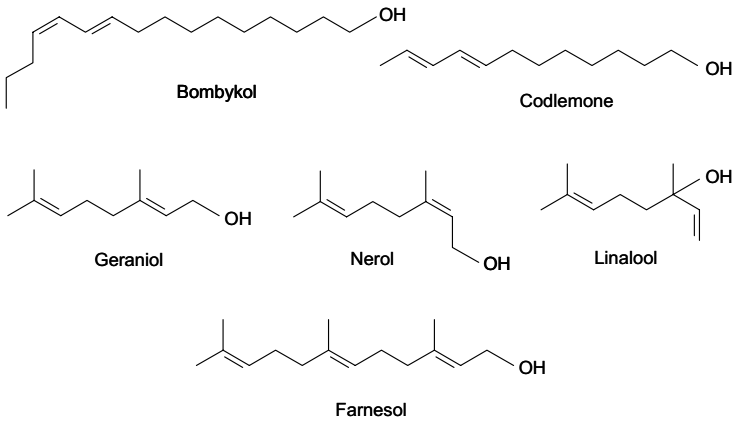

Fig. 2. Some higher fatty acohols with two or more double bonds

portant starting compound for organic synthesis. Farnesol is a natural pesticide against mites and is a pheromone for several other insects (Lapczynski *et al*., 2008). Farnesol is used as a deodorant in cosmetic products because of its anti-bacterial activity (Kromidas *et al*., 2006). On the other hand, it is a subject of discussed restrictions on its use in perfumery as some people may become sensitised to it, however, the evidence that farnesol can cause an allergic reaction in humans is still controversial (Gilpin and Maibach, 2010). Additionally, farnesol has been suggested to function as a chemopreventive and anti-tumor agent (Joo and Jetten, 2009).

Two chlorinated derivatives of unusual alcohols were described in a red alga *Gracilaria verrucosa* (Shoeb and Jaspars, 2003). Both compounds have a C12 aliphatic chain chlorinated in position 2 and with one double bond at carbon 2 (2-chlorododec-2-en-1-ol) or two double bonds at carbon 2 and 11 (2-chlorododec-2,11-dien-1-ol).

ALCOHOLS WITH TRIPLE BONDS (Fig. 3)

Synthetic acetylenic alcohols are substances used as components for organic syntheses. Natural acetylenic alcohols and their derivatives have been isolated from a wide variety of plant species, fungi and invertebrates. Pharmacological and toxicological studies have revealed that many of them display chemical and medicinal properties.

From the synthetic acetylenic alcohols, only 2-propyn-1-ol (***propargyl alcohol***) (CAS 107-19-7) represents a chemically important and toxicologically explored alcohol containing an alkyne functional group. It is clear colorless viscous liquid that is miscible with water and the majority of polar organic solvents. It is insoluble in hydrocarbon solvents. Propargyl alcohol is used as a corrosion inhibitor, a metal complex solution, a solvent stabilizer and as an electroplating brightener additive. In addition, it is used as an intermediate in organic synthesis.

3-Butyn-1-ol (CAS 927-74-2) and ***4-pentyn-2-ol*** (CAS 2117-11-5), primary and secondary homopropargylic alcohols, displayed 320 and 160 times more toxic effect, respectively, than predicted. In this case an activation step involving biotransformation to an allenic electrophile intermediate was proposed (Veith *et al*., 1989).

Few monoacetylenic alcohols, as for example ***4-decyn-3,6-diol***, were isolated from a culture of *Clitocybe catinus* (*Basidiomycetes*) and subsequent study of their structure revealed the presence of two or three hydroxyl groups (Arnone *et al*., 2000).

Devil's club (*Oplopanax horridus*) has been revealed as a rich source of diacetylene alcohols being probably the most important spiritual and medicinal plant to most indigenous tribes who live within its habitat. Different parts of this plant are used by over 38 linguistic groups for over 34 categories of physical ailment, as well as for many spiritual applications (Lantz *et al*., 2004). From this plant, substances such as ***falcarindiol*** (9-heptadecadiene-4,6-diyne-3,8-diol) (CAS 55297-87-5), ***oploxyne A*** (9,10-epoxy-heptadeca-4,6-diyne-3,8-diol), and ***oploxyne B*** (10-

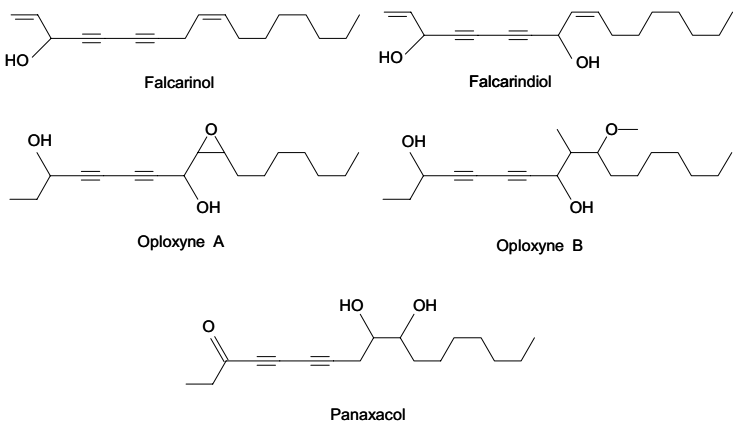

Fig. 3. Some higher fatty acohols with triple bonds

methoxyheptadeca-4,6-diyne-3,8,9-triol) were isolated (Yang *et al*., 2010; Yadav *et al*., 2011). Falcarindiol induces phase II drug-metabolizing enzymes, blocks carbon tetrachloride-induced hepatotoxicity in mice through suppression of lipid peroxidation (Ohnuma *et al*., 2011), allosterically modulates GABAergic currents in cultured rat hippocampal neurons (Wyrembek *et al*., 2012) and preferentially kills colon cancer cells unlike normal colon epithelial cells. Furthermore, falcarindiol inhibits tumor growth in a xenograft tumor model and exhibits strong synergistic effect on cancer cells with 5-fluorouracil, an approved cancer chemotherapeutic drug (Jin *et al*., 2012).

Falcarinol (1,9-heptadecadiene-4,6-diyn-3-ol) (CAS 21852-80-2), was firstly isolated from *Falcaria vulgaris* (Bohlmann *et al*., 1966), later from Korean ginseng (Matsunaga *et al*., 1990) and also from carrot (Zidorn *et al*., 2005). Falcarinol has potent anticancer properties on primary mammary epithelial cells (Christensen *et al*., 2011). These results might be important in developing new anticancer therapy with simple and common vegetables. At high concentrations, falcarinol is capable to induce contact dermatitis (Machalo *et al*., 2002).

Panaxacol ((9*R*,10*R*)-9,10-dihydroxyheptadeca-4,6-diyn-3-one) (CAS 106828-96-0) and ***dihydropanaxacol*** ((9*R*,10*R*)-heptadeca-4,6-diyne-3,9,10-triol) (CAS 124989-71-5) are cytotoxic polyacetylenes isolated from the callus of *Panax ginseng* (Fujimoto *et al*., 1990). Specifically these chemically similar and antimicrobially active compounds were isolated from *Panax ginseng* hairy root culture (Fukuyama *et al*., 2012).

ALCOHOLS WITH BOTH DOUBLE AND TRIPLE BONDS (Fig. 4)

Many polyacetylenic alcohols were found in primitive marine organisms, such as ascidians and sponges. Sponges produce a variety of secondary metabolites and are considered as a gold mine for the chemists. These invertebrates have no physical defenses and thus they have developed efficient chemical mechanisms such as polyacetylenic metabolites to resist predators and bacteria.

Acetylenic alcohols with a long linear carbon chain (38 carbons) have been also described in sponges, specifically in a tropical sponge *Reniochaline* sp. (Lee *et al.*, 2009). These exhibited a significant growth inhibiting effect against human tumor cell lines. A similar linear polyacetylene alcohol (36 carbons) named ***lembehyne A*** found in Indonesian marine sponge *Haliclona* sp. (Aoki *et al*., 2001) exhibited the ability to induce neuronal differentiation in neuroblastoma cells (Aoki *et al*., 2003). Newly synthesized LB-18, closely related to lembehyne A has been shown to induce p21/WAF1 and cause G1 phase arrest in mouse neuroblastoma Neuro2A cells and thus cause cell death in human neuroblastoma KP-N-TK cells in a dose-dependent manner (Ozimi *et al*., 2006).

Several polyacetylenic alcohols with 22 carbon chain were isolated and described in lipid extract from a Red Sea sponge, *Callyspongia* sp. (Youssef *et al*., 2003). They include callyspongines A and B (Rooney and Capon, 1998) and callyspongenols A-C (Youssef *et al*., 2003), by way of example. Their physical study revealed presence of 4 triple bonds

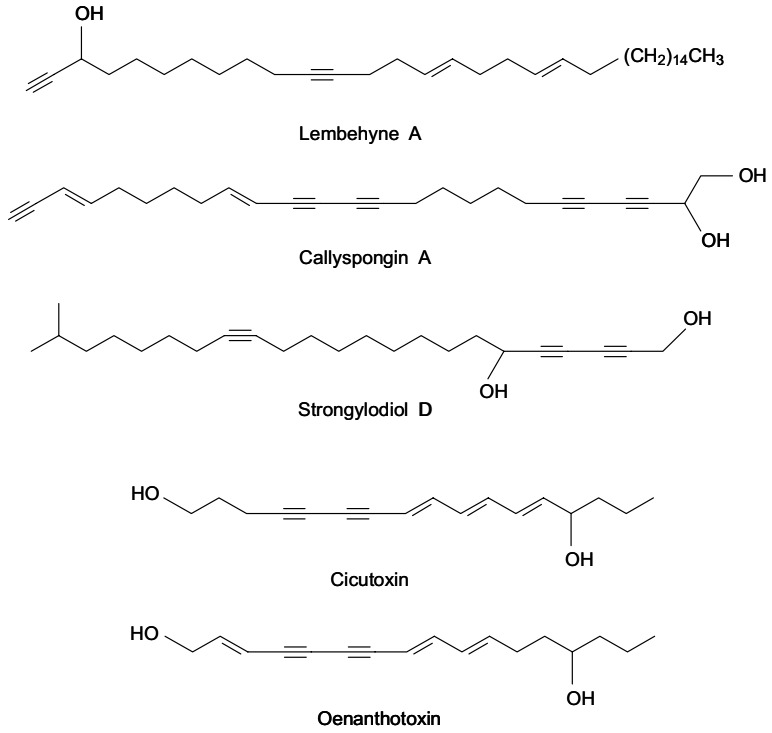

Fig. 4. Some higher fatty acohols with double and triple bonds

and one, two or three double bonds. ***Callyspongin A*** ((2R,14Z,20Z)-14,20-tricosadiene-3,5,10,12,22-pentayne-1,2-diol) from *Callyspongia truncata* inhibits the growth activity of starfish egg, MIC 6.3 μmol/L.

Strongylodiols are long-chain di- and tri-acetylenic di-alcohols with a chain of 26 up to 31 carbon atoms. Strongylodiols A, B and C were isolated from a *Petrosia* Okinawan marine sponge of the genus *Strongylophora* (Watanabe et al., 2000), later other strongylodiols - strongylodiols D−J – were isolated and described (Watanabe *et al*., 2005). Strongylodiols exhibit cytotoxic activity (Kirkham *et al*., 2004).

Cicutoxin (8,10,12-heptadecatriene-4,6-diyne-1,14-diol) (CAS 505-75-9), the poisonous principle of the genus *Cicuta*, is a violent neurotoxin causing convultions and respiratory paralysis (Starreveld and Hope, 1975). It is one of many toxic polyacetylenes, which were found in aerial and subterranean parts of water hemlock (*Cicuta virosa* L.). It is well known that water hemlock tubers and leaves are highly toxic to animals and to humans (Wittstock *et al*., 1997; Heath, 2001; Schep *et al*., 2009). Cicutoxin is a potent K+ current blocker which inhibits K+ channel-dependent proliferation of naive and memory T lymphocytes (Strauss *et al*., 1996).

Oenanthotoxin ((2E,8E,10E,14R)-heptadeca-2,8,10-triene-4,6-diyne-1,14-diol) (CAS 20311-78-8) and ***dihydrooenanthotoxin*** ((8E,10E,14R)-heptadeca-8,10-diene-4,6-diyne-1,14-diol) (CAS 20312-71-4) are toxic polyacetylenic alcohols from the roots of Sardinia plant *Oenanthe fistulosa* (Rhazi *et al*., 2012). Representatives of the *Oenanthe* genus (*Umbelliferae* family) belong to the most poisonous species of the European flora. These plants share some kind of similarity with parsnip and carrot and for this reason they are a frequent cause of fatal human poisonings (Brunetin, 1999). Sardinian *Oenanthe* species have special ethnopharmacological relevance, being considered as the most likely candidate for the famous sardonic herb, a neurotoxic plant used in pre-Roman Sardinia for the ritual killing of elderly people (Ribichini, 2000). According to Appendino *et al*. (2009), elderly people unable to ensure themselves were intoxicated with the sardonic herb and then killed by pushing down from a high rock or by beating to death. The facial muscular contraction induced by the sardonic herb mimicked a smile, and the expression *risus sardonicus* (sardonic smile) indicating a sin-

ister smile is well documented in the Latin and Greek literature and in the majority of modern European languages. It even found its way into the medical lingo as the expression for a lockjaw (*trismus*), the spasm of the mastication muscles (Farrar *et al*., 2000).

Oenanthotoxin is an isomer of cicutoxin isolated from a water hemlock (*Cicuta virosa L*.), with the only difference in the position of a single double bond, located next to the secondary oxymethine in cicutoxin and adjacent to the primary hydroxyl in oenanthotoxin (Anet *et al*., 1952, 1953). Recently it has been revealed that oenanthotoxin and other polyacetylene compounds downregulate GABAergic currents (Appendino et al., 2009), induce open channel block and allosterically modulate $GABA_A$ receptors (Wyrembek *et al*., 2010).

CONCLUSION

Unsaturated aliphatic alcohols are found in nature and may also be used in organic synthesis, especially in making flavors, pharmaceuticals, insect repellents and insecticides. These alcohols have a lot of various applications and may be toxic if ingested in large enough quantities. Some of the smaller alcohols are metabolized by organisms via alcohol dehydrogenase to form more toxic metabolites.

Unsaturated aliphatic alcohols also occur in nature in many forms and have many functions. Some serve as semiochemicals, others as a protection against predators. Some natural unsaturated alcohols exhibit a variety of biological activities, such as toxicity, including in humans.

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