A review on ambergris perspective and modern chemical composition and pharmacology

Accepted 28th July, 2020

ABSTRACT

Ambergris is the pathological (the only source) secretion of the intestine sperm whale *Physeter macrocephalus* syn. *Physeter catodon* belonging to the family Physeteridae. Ambergris has been found only rarely for centuries, as jetsam on beaches all over the world known as Baltic amber. Ambrein is the major constituent of ambergris and responsible for its various pharmacological activities like breakdown of the relatively scentless ambrein through oxidation produces ambroxan and ambrinol, the main odor components of ambergris. Other amber originated from pine plants resin known as *sucinum*; other amber known as compressed amber, made of small pieces and small stones that melted together under high pressure.

Key words: Ambergris, amber, sperm whale, ambrein, chemistry, pharmacology.

INTRODUCTION

Ambergris or Baltic amber, is an amber that is not specific in color or shape and originates in the Baltic region throughout the past 5,000 years, most of the amber in the world has come from the Baltic Sea called the amber coast, real amber, a term that includes natural Baltic amber of which do not contain any additives and the amber ratio is 100% (Dannenfeldt, 1982; Dharmananda, 2020). Nowadays, the majority of the world’s amber has come from a more limited portion of the Baltic, the Kaliningrad Oblast, a Russian sea port area between Poland and Lithuania (Dannenfeldt, 1982). Ambergris when it is fresh is black and mixed with blood and fecal matter and has unpleasant odor, then the mass exposed to the air and sun, ambergris become light gray, hard and has sweet musky odor (Dannenfeldt, 1982). Ambergris is not known in the classical Greeks and Romans era, and the absence of European tradition resulted in wide speculation. According to a Greek legend, sun rays hit the ground during the sunset hours and give birth to a fluid that after dropping in the ocean is transformed into amber, which can be collected onshore. Amber was called elektron by ancient Greeks, meaning “shining thing”, from which the term “electricity” was coined (Ragazzi, 2016). The Romans used to call amber *sucinum* (Latin term for a substance that is ultimately derived from sap or juice), because they learned it was a juice of a tree, that is, a true resin of old pines, growing in the regions touched by the northern ocean. Among the many other hypotheses on the origin of amber, ambergris is called by Germans glesso (from this term comes the modern English term “glass”), originating in the “Glessaria” islands in the Northern Sea and it flows from pine-like trees (Ragazzi, 2016; Gode, 1949; Kemp, 2012). Amber, *ambra* in Italian also succino or carabe in Medieval time, from the fact that amber has been found very often on the shore of the Baltic sea, after being eroded from undersea deposits and therefore believed as a material originated from the sea. The property of attracting lightweight objects after rubbing amber suggested the Persian name *karabe*, “straw
Ambergris is a coprolite originating from the sperm whale *Physeter macrocephalus* Linnaeus, synonym *Physeter catodon* Linnaeus, belonging to the family Physeteridae (Gode, 1949, Kemp, 2012). Ambergris has been found only rarely for centuries, as jetsams on beaches all over the world. The name ambergris is of French origin from the combination of two words: *ambre* (amber) and *gris* (gray), as a way to describe its appearance (Kemp, 2012). Ambergris has been known since antiquity with Arabs and Chinese first using it for perfumery or to burn as incense. In Arabic is known as “Anbar” is a solid substance that has no taste and no smell unless it is crushed or burned, and it gives off a pleasant smell (Al-Jabiry, 1999). Ambergris forms only in the intestines of the sperm whale, mainly found in the large intestine or rectum. Franz Xavier Schwediawer described ambergris in 1783 as “preternaturally hardened whale dung” (Kemp, 2012). Squids are the main source of food of sperm whale, and when their beaks block their duodenum, the intestinal wall absorbs water from the feces-impregnated mass causing solidification. As time goes by, the mass grows by accretion (Kemp, 2012). The resulting material ends up having an irregular shape, a waxy nature. Although they look solid, ambergris pieces float once they are expelled because their specific gravity is lighter than water (0.73–0.95). Though they have been described many times as “whale vomit” (Kemp, 2012; Ragazzi, 2016). Ambergris is rather rare and may be found in only a few sperm whales (1%) in both males and females. The ambergris pieces are most likely defecated or just released in the ocean when they become too big and kill the sperm whale because of intestinal obstruction. Once the whale dies, the ambergris pieces just float on the ocean, most pieces of ambergris have been collected directly from sperm whale intestines that have been caught in whaling operations. In color they are pale yellowish to light gray on the inside, while the outer surface is dark brown with a varnished appearance (Kemp, 2012; Rice, 2009; Ragazzi, 2016). Fresh ambergris has the highly distinctive pungent odor of sperm whale feces, its odor changes according to the time it has been exposed to air, but aged pieces have an almost pleasant musty or even musky smell. It is not indispensable to the perfumery industry nowadays, ambergris applied for its fixative properties for perfumery (Rice, 2009; Ragazzi, 2016).

**MATERIALS AND METHODS**

All the available information on Ambergris was collected from Ibn Rushd Book “Kulliyat Fi A-Tibb, Colligit” and via a library and electronic search (using Web of Science, Pubmed, SciFinder, Scopus, Google Scholar...etc.).

**RESULTS AND DISCUSSION**

**Traditional medicinal uses of ambergris**

Because of its unique odor it was used in Europe during the
plague to “sanitize” the air, which was believed to be at the root of the epidemic. Some also used it as an aphrodisiac and for various medicinal purposes (Kemp, 2012). Ambergris was thought to be used as a remedy for hydrophobia, epilepsy, typhoid fever, asthma and various nervous diseases (Read, 2013). The Andalusian philosopher Ibn Rushd (1128-1198 A.D.), known in west by the name of Averroes. Ibn Rushd was a faithful disciple of Aristotle and he stuck to the organization of the Aristotelian corpus implemented by Andronicus of Rhodes. He wrote many books in natural physics, philosophy and in addition one book in medicine known as “Kulliyat Fi A-Tibb, known in its Latin translation as Colliget (Al-Jabiry, 1999). Ibn Rushd mentioned the medicinal uses of ambergris as a tonic to the heart, brain, stomach and senses. It is useful for the elderly and the cooled patients. It is beneficial for cold, stomach aches, flatulence of large intestine and from the cough and if painted topically, it strengthens the organs, especially nerves and used during the plague to “sanitize” the air, which was responsible for the mass death” (Al-Jabiry, 1999). It has been used by Ancient Egyptians for scenting cigarettes, in Yemen and other Arabic countries, ambergris has been used in folk medicine for gaining weight and as aphrodisiac (El-Sayed et al., 2012). Ambergris, which is commonly used as an analgesic in the Saudi folklore medicine (Taha, 1992). In Mexico people use amber necklaces against the “aire”, a disease considered to be caused by wind, according to a common belief among populations of South America and linked to ancient Aztec medicine a gold-colored amber, wearied on the neck, is able to heal fever and other illnesses (Ragazzi, 2016). Amber teething necklaces supposedly provide analgesia for teething infants (Machet et al., 2016; Catherine et al., 2017). To prevent the disease, amber was also recommended as amulet, rubbering wrists often with it or die of plague (Kemp, 2012).

Chemical composition of ambergris

Ambergris is the pathological (the only source) secretion of the intestine sperm whale. The whale that produced ambergris may not be sick, healthy ones also produce ambergris. Squids are the main food of sperm whale and may likely play some part in the formation of ambergris (Kemp, 2012). Ambergris is produced in vivo in about 1% of Sperm whales Ambrein C_{30}H_{52}O, 1-ambra-8, 13, 18- triene, is the major constituent (up to 97%) of ambergris with co-occurring variable proportions of steroids, some kinds of squids contain ambrein which is present in the ambergris (Dees, 1961; Rowland et al., 2017). It is noted that ambrein is either obtained directly from the intestine sperm whale or from the jetsam (Rowland et al., 2017). Analyzing 85 years old sample of ambergris from New Bedford Whaling Museum (MA), by using adsorption chromatography and 1H spectroscopy (FT-NMR). The results showed that ambrein is the major compound of ambergris, even after 85 years (Moniz et al., 1996). Various samples of jetsam were examined by analytical methods such as gas chromatography-mass spectrometry (GC-MS), then the radiocarbon ages of some of the samples by well-described accelerator-MS techniques was determined. Some samples of jetsam have remained in the environment for about a thousand years (Rowland et al., 2019). Breakdown of the relatively scentless ambrein through oxidation produces ambroxan and ambrinol, the major odor components of ambergris (Kemp, 2012 ; Rowland et al., 2019). Other synthetic compounds used in perfume industry, ambroxol, based on the ambrinol and ambroxol structure.

Application of solid phase micro extraction (SPME) and gas chromatography-mass spectrometry (GC-MS) to analysis of the volatiles and semi-volatiles of jetsam ambergris from New Zealand, likely recently ejected from a sperm whale, revealed traces of volatile/semi-volatile compounds γ-dihydroionone, C_{13}H_{22}O, and odor-free pristane, C_{15}H_{30}, as the major constituents (Wilde et al., 2019). Other constituents of ambrein derivatives are several sterols, up to 46%, Epi coprostanol, coprostanol, coprostanone, and traces of cholesterol. The fatty acids of ambergris show to be composed mainly of stearic acid, oleic, linoleic, arachidonic, and behenic acids (Taha 1989a, 1989b). Pine resin contains a number of aromatic compounds: the terpenes, such as pinene, carene, sabinene, limonene, which may be lost during the period of aging to become amber. These compounds found in pine resin are either pure hydrocarbon (pinene is an example of a pure hydrocarbon, containing only carbon and hydrogen), or hydrocarbons with small amounts of oxygen. In a single study of Baltic amber reported in 1877 but repeated by most modern authors, it was said to have 3-8% succinate (succinic acid), which is probably a derivative of the original simple terpenes (Dharmananda, 2020). It is clear that pine resin amber rich in typical mono- and sesquiterpenoids responsible for the odor of the plant amber resin.

Pharmacology of ambergris

The many properties of amber for internal use are enumerated, it was used against (head diseases, humid
diseases of the head) and also to treat catarrh, epilepsy, apoplexy, dizziness. It was reported to be effective against asthma, cough and all the most serious diseases of the lung, it was believed useful to cure urinary retention caused by painful kidney stones (Kemp, 2012; Rice, 2009). Amber was not only a gemstone very appreciated by ladies, by wearing it as a necklace or as other jewels, but it was also used to cure woman’s diseases, amber t induces menstruation and is effective in solving womb spasm (Moniz et al., 1996; Kemp, 2012). Moreover, it was thought useful in difficult labor since powdered amber, mixed with white wine, seemed to make childbirth easier and faster. There is no disease of the stomach, gut, nerves, and mostly brain that amber dissolved in wine cannot heal. A reason for the success of this treatment with amber probably depended just on the healthy life of amber fishermen working along the Baltic shore, preventing in this way the infection, spread out by fleas of rats in crowded cities (Rice, 2009; Ragazzi, 2016; Rowland et al., 2017). Amber was much-sought for this use until the middle of 19th century, but with the beginning of the modern medicine, its use disappeared carrying with it the memory of ancient times (Kemp, 2012), this is due to the progress in medicine and knowing more about diseases. Chinese amber is ground to powder and swallowed down with water, as a decoction, powder, pills or extract of herbs that make up a formula with the succinum, with a typical dose 1.5-3.0 grams for one day. Succinum is used in the treatment of palpitation, amnesia, dreaminess, insomnia, epilepsy, urinary disorders, modern formula developed for the treatment of kidney and bladder stones with blood in the urine; another formula with various herb used as decoction, succinum was added for its s used in treating stomach ache.

Succinum can be used topically for promoting tissue regeneration (Dharmaransa, 2020; Chatterji et al., 2010). Although the scientific basis of these substances was not understood, Aphrodisiacs were valued for their ability to enhance the sexual experience and have been dated back thousands of years in Chinese, Indian, Egyptian, Roman, and Greek cultures many substances used include ambergris and according to Arabic traditional medicine amber can be used as an aphrodisia (Melnyk et al., 2011; Rodrigues, 2000). The mode of action of aphrodisiac is to increase libido, potency or sexual pleasure. Ambrein is used in the Arab countries for increasing libido by increasing the concentration of several anterior pituitary hormones and serum testosterone (Sandroni, 2001). Dr. Sadek Taha and coworkers have published several scientific papers in which they report the activities and the effects of ambrein, the main constituent of ambergris. The LD₅₀ of ambrein, given intraperitoneally (i.p.) in mice, was found to be high (7.5 g/kg), and ambrein proved to be a safe compound in this species (Taha, 1992). Ambrein did not cause any toxic symptoms in the liver, did not affect the plasma protein, cholesterol, glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase profiles but lowered alkaline phosphatase at high doses after subacute treatment (Taha et al., 1995). Ambrein was studied on the sexual behavior of male rats. Ambrein produced recurrent episodes of penile erection, a dose-dependent, vigorous and repetitive increase in intromissions and an increased anogenital investigatory behavior, indicating the ambreinis as a sexual stimulant (Taha et al., 1995). Ambrein was found to possess antinociceptive activity in mice at doses which did not sedate or incapacitate the animals. The antinociceptive activity of ambrein was inhibited by a noradrenergic neurotoxin and by naloxone, methysergide or prazosin. It was not influenced by a serotonin depletor, p-chlorophenylalanine (Taha, 1992). Ambrein increased prothrombin time, partial thrombin time and thrombin time and decreased fibrinogen levels ambrein showed anticoagulant and antifibrinocogenic activities (Taha et al., 1995). Ambrein reduced the blood glucose level of normal and moderately alloxa-diabetic rats but did not reduce the blood glucose levels of severely-diabetic rats. Results suggested that the hypoglycemic activity of ambrein may be mediated by enhanced glucose utilization (Taha, 1991). Ambrein-induced non-selective dose-dependent antagonism to the effects of some agonists (acetylcholine, adrenaline, noradrenaline, prostaglandins and oxytocin) in some smooth muscles may be due to the ability of this compound to interfere with the mobilization of extracellular Ca²⁺ required for muscular contractions induced by these agonists (Taha et al., 1998). Epi coprostanol (3α-hydroxy-5β-cholestanol) has been studied for its effects on blood glucose and plasma insulin levels in rodents. Epi coprostanol significantly induced hypoglycemia and increased insulin levels in rat blood plasma, in a dose dependent manner. In contrast, diabetic animals suffering from insulinitis showed a significant decline in hyperglycemia, strongly suggesting an insulin-like action of Epi coprostanol, most likely that Epi coprostanol acts through a mechanism other than hyperinsulinemia (Taha and Raza, 1996). Epi coprostanol, possess anti- activity against carrageen an induced edema in rat paw in a dose dependent manner. Epi coprostanol achieves it's anti-inflammatory effects, by inhibiting kinins and prostglandins effects. Epi coprostanol showed that anti pyretic effect, might be the effect of Epi coprostanol through chemical neuro modulators (dopamine, acetylcholine and serotonin). Epi coprostanol,like ambrein, did not reduce the animal activities nor induce sedation.
during the study (Taha et al., 1994). Amberin and Epi coprostanol were evaluated for their antioxidant potential in vitro as well as in vivo. The results showed that ambrein behaves like antioxidant in vitro studies but the same time it decreased non-protein sulphhydryl contents in vivo accompanied by a decline in malondialdehyde contents. Whereas, Epi coprostanol showed a possible antioxidant potential effects (Raza et al., 2007). A total of forty subjects were recruited to receive randomly 415 mg/day of either ambergris for 4 weeks, results show significant increase in testosterone, estradiol, prolactin, insulin, cortisol, thyroxin levels and body weights, while growth hormone showed non-significant changes. A significant increase in total cholesterol, low density lipoprotein cholesterol and high density lipoprotein cholesterol, while significant decrease in triglycerides levels in ambergris group were observed, concluded that ambergris ingestion resulted in increase of both sexual desire and body weights due to its effect on some endocrine hormones (El-Sayed et al., 2012). Amber teething necklaces to prevent teething pain in infants. Bacterial colonization of amber necklaces worn by children during hospital consultations revealed the presence of 32 different species, the most frequent being coagulase-negative staphylococci (Staphylococcus epidermidis in 88.9% of cases). In three cases, methicillin-sensitive Staphylococcus aureus was found, these bacteria are saprophytes and they may become pathogenic in particular conditions (Machet et al., 2016, Catherine et al., 2017).

CONCLUSION

The results give further insights into the chemical compositions, pharmacological activity and beneficial effects of Ambergris. The results showed that the amber drug is safe to be used in folk medicine with major property as aphrodisiac and gaining weight drug.

ACKNOWLEDGEMENT

This paper was not supported by any financing or grants. I would like to thank the librarians at the library of Jordan University of Science and Technology (JUST) for their great help during the preparation of this manuscript.

REFERENCES


APPENDIX

Ambreinγ-DihydroiononePristane

Ambroxan Ambrinol

Epi coprostanol