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Use of Molluscs in Spasmodic Pain

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ABSTRACT

Muricidae, a family of marine mollusks, has a lot of potential as a source of therapeutically beneficial chemicals. These mollusks are most known for producing the old color Tyrian purple, but they also serve as the basis for a number of rare traditional medicines that have been utilized for thousands of years. While the biological activity of extracts and chemicals from these snails has not been chemically examined or tested for efficacy in controlled clinical studies, a large amount of independent research has revealed the biological activity of these snails. Muricidae, in particular, create a variety of brominated indoles with anti-inflammatory, anti-cancer, and steroidogenic activities, as well as choline esters that relax muscles and relieve pain. Some of the historic usage in wound healing, stomach pain, and menstrual difficulties could be explained by these substances. The hypobranchial gland, on the other hand, is the primary source of bioactive substances, although the shell and operculum are the primary sources employed in most traditional cures. As a result, more research is needed to clarify this discrepancy and to improve a quality-controlled natural medication from the Muricidae family.

Keywords: Whelk, Indoles, Choline Esters, Ethnomedicine, Marine Natural Products

Introduction

Although plants provide the majority of natural medicines, marine invertebrate groups, such as the Mollusca, are gaining popularity as a source of novel bioactive chemicals. Purified or synthesised bioactive chemicals have been developed as medicines, while crude or semi-purified extracts have been developed as nutraceuticals, with marine mollusks being employed for a variety of therapeutic uses. Traditional Chinese, Indian, South African, and Middle Eastern medicines, as well as homeopathic cures, use a variety of marine mollusks. Mollusks that are eaten directly may help to prevent disease by delivering vital nutrients, as well as immunostimulatory chemicals and other secondary metabolites with direct biological activity.

The bioactive characteristics of extracts and secondary metabolites from the Muricidae family of marine gastropods are reviewed in this research. Muricidae, also known as murex or rock whelks, have a long history of pharmacological use, with Dioscorides listing them in the Materia Medica in the first century AD, Arabic scholars reporting them in the ninth century, and medieval Jewish pharmacies selling them from the eleventh to fourteenth centuries AD. Traditional Chinese medicine (TCM), which has been practiced for over 3500 years, uses a number of Muricidae species. Muricids' purple secretion is also the basis for a homeopathic medicine that has been used in clinical practice for over 150 years. These Muricidae medications are used to treat a wide range of ailments, with some common themes including menstruation issues, wounds, ulcers, and pain relief. However, there are no scientifically rigorous studies examining the efficacy or safety of any CAMs that we are aware of. However, a large body of independent study has been conducted on the bioactive secondary metabolites and haemocyanins from specific Muricidae species, and some of these substances may add to traditional medical applications. We study the bioactivity of muricid natural products in depth, then outline the present biomedical applications of muricid CAMs, and assess if the existing CAM applications are potentially substantiated by the presence of pharmaceutical molecules. This analysis shows the potential for future development of a new scientifically-based nutraceutical from Muricidae molluscs, as well as some of the constraints in coupling CAMs with bioactive components from the source species. While the biological activity of extracts and chemicals from these snails has not been chemically examined or tested for efficacy in controlled clinical studies, a large amount of independent research has revealed the biological activity of these snails. Muricidae, in particular, create a variety of brominated indoles with anti-inflammatory, anti-cancer, and steroidogenic activities, as well as choline esters that relax muscles and relieve pain. Some of the historic usage in wound healing, stomach pain, and menstrual difficulties could be explained by these substances. The hypobranchial gland, on the other hand, is the primary source of bioactive substances, although the shell and operculum are the primary sources employed in most traditional cures. As a result, more research is needed to clarify this discrepancy and to improve a quality-controlled natural medication from the Muricidae family.

Steroidogenic Effects of Muricidae Extracts and Analogue Compounds

The continued usage of Muricidae traditional medicines to address women's ailments (described below) suggests that they may have steroidogenesis-related effects. The production of steroid hormones is essential for the menstrual cycle, the growth and creation of mature oocytes, and the

establishment and maintenance of pregnancy. The steroidogenic pathway is found in the granulosa cells of the ovary, as well as uterine and placental cells in women.

Low doses often enhance steroidogenesis, while high levels decrease it. D. orbita extracts, on the other hand, appear to have an uncommon inverse hormetic reaction on P4 synthesis (i.e., inhibition at low doses and stimulation at high doses over a narrow dose range).Edwards et al. investigated the effects of D. orbita extracts and compounds on progesterone and estradiol synthesis in granulosa cells, both with and without hCG. In addition, the effects of different synthetic isatin and indirubin compounds on basal progesterone synthesis in granulosa and JAr cells were investigated. Because cytotoxicity has an effect on steroidogenesis and secretion, only non-cytotoxic dosages of Muricidae substances are taken into account in. The comparison of semi-purified compounds with crude D. orbita extracts reveals that certain brominated indole derivatives have a particular and targeted activity. Tyrindoleninone appears to have no effect or be inhibitory on basal and hCG-stimulated progesterone synthesis, but it does elicit an n-shaped dose response curve in basal and hCG-stimulated estrogen synthesis. Tyrindoleninone promoted estrogen synthesis at low doses but not at high quantities, but had no effect on progesterone synthesis. This shows that after progesterone generation, tyrindoleninone may operate on estrogen biosynthesis pathway targets. The effects of 6-bromoisatin on granulosa cell steroidogenesis were inconsistent, and further evidence is needed to characterize this compound's steroidogenic activities. Nonetheless, these preliminary findings show that Muricidae extracts and compounds have the ability to inhibit or reduce steroidogenesis.

Effect of Muricidae extracts and synthetic analogue compounds on basal and gonadotrophin-stimulated progesterone and estrogen synthesis in vitro.

Muscle Relaxing and Nicotinic Activity of Choline Esters

Muscle relaxing characteristics with nicotinic action have been found in hypobranchial gland extracts from a variety of muricid species, with choline esters being the main contributors. Choline esters can be found in the polar part of organic solvent extracts and are soluble in ethanol, methanol, acetone, and to a lesser extent, water. The frog rectus experiment was used to establish similarities in the pharmacological effects of gland extracts and choline esters in vitro. These chemicals impede neuromuscular transmission but do not bind to muscarinic acetylcholine receptors, indicating that they have a high affinity for nicotinic cholinergic ligand-gated ion channels. At doses of 3 mg/kg, Keyl and Whittaker (1958) were able to assess depolarization on the endplate region of rat gracilis muscle, indicating that murexine may bind to nicotinic acetylcholine receptors. Murexine's effect on twitch reduction was also studied in vitro on the gastrocnemius muscles of cats, dogs, and rabbits. Murexine, dihydromurexine, and senecioylcholine in vivo studies back up the neuromuscular blocking activity reported in vitro in the frog rectus experiments. In rabbits, all three choline esters caused head droop, while in dogs, all three choline esters caused back leg paralysis. Clinical experiments on 160 human patients found that a single dose of 1 mg/kg of murexine resulted in 3–6 minutes of muscle paralysis, whereas a gradual i.v. infusion of a 1/1000 solution of murexine in physiological saline resulted in longer-lasting muscular relaxation.

Muricidae extracts and chemicals have neuromuscular and pain signaling effects; (a) Choline ester and hypobranchial gland (HG) muscle relaxing and nicotinic activity; (b) Isatin derivative neurotransmitters, analgesics, and sedative characteristics

When compared to other muscle relaxants such as decamethonium, suxamethonium, gallamine, and tubocurarine, the muricid choline esters have the most dosage and effect similarities to suxamethonium, a depolarizing kind of neuromuscular blocker. Murexine and other muricid choline esters have a variety of structural properties that affect their efficacy as muscle relaxants, including the electron density of the "ether" oxygen atom and the quaternary ammonium ion (O(CH2)3N+(CH3)3 group) (Figure 2c), which is comparable to acetylcholine. These structural characteristics may explain the muricid choline esters' nicotinic activity, as they appear to replicate acetylcholine's action on nicotinic acetylcholine receptors, albeit this connection has yet to be proven. Low doses have minimal effect on respiration and blood pressure, however large doses above 100–200 mg/kg raise blood pressure and respiration in anaesthetized cats and dogs, showing sympathetic ganglion activation in addition to neuromuscular blocking activities. Humans have adverse effects such as nausea and vomiting as a result of nicotinic action. This was reported in certain participants in a murexine clinical trial, discouraging further research or uses with this substance.

CONE SNAIL

The critter in question is a cone snail, a mollusk well-known among beachcombers and marine biologists for its poisonous venom, which has lately been turned into a painkiller. The cone snail is just one illustration of the pharmaceutical industry's benefits from global biodiversity.

The cone snail is well-known in the mollusk world because of its lethal venom, which was first investigated in the 1960s by Baldamero Olivera, who is currently a scientist at the University of Utah. Olivera found a molecule in the toxin in the early 1980s that has the same pain-killing qualities as morphine but is 1000 times more effective. Ziconotide, a medication derived from the chemical, was licensed in 2004 for the treatment of chronic and persistent pain caused by AIDS, cancer, and neurological illnesses. It's far from the only therapeutically employed biological medication (see salmon and sea sponges), and it's certainly not the first to come from a venomous creature: Exenatide, an investigational Type 2 diabetes medication, was created using an enzyme found in the venom of the Gila monster.

However, Olivera believes that the cone snail may have something more to offer in terms of medications. Only a few years after the discovery of Ziconotide, Olivera discovered residues of a compound in the cone snail that did not appear to be produced by the mollusk. Eric Schmidt, a medicinal chemist at the University of Utah, adds, "He indicated he had a feeling there was some kind of symbiotic bacterial component that might be involved here." Olivera enlisted the help of Margo Haygood, a marine microbiologist and researcher at Oregon Science and Health University, to see if the foreign substance was left behind by small microbes living inside the cone snail.

CONCLUSION

Painkillers, which merely provide symptomatic relief, can be substituted with the biochemical extract found in these mollusks. To prove the efficacy of the mollusk compound in treating spasmodic pain and other muscular discomfort, more research is needed.