REVIEW ARTICLE

Annals of Agricultural and Environmental Medicine
www.aaem.pl

The potential of ancient medicine – using products from snails in treatment of oncology patients

Krzysztof Piotr Jasik[1,A,D,F] ✉, Jan K Kinasiewicz[2,B,D], Szymon Szlęzak[2,B-C], Jarosław Paluch[3,C,E-F]

[1] *Department of Medical Sciences, Collegium Medicum, Jan Długosz University, Częstochowa, Poland*
[2] *Collegium Medicum, Jan Długosz University, Częstochowa, Poland*
[3] *Department of Laryngology, SPSK A. Mielęckiego Medical University of Silesia in Katowice, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Jasik KP, Kinasiewicz JK, Szlęzak S, Paluch J. The potential of ancient medicine – using products from snails in treatment oncology patients. Ann Agric Environ Med. doi: 10.26444/aaem/206989

Abstract

Introduction and Objective. Although routine treatment methods aim to aggressively destroy tumour tissues, they often fail to account for the correlations of tissue destruction and regeneration processes. Despite considerable progress in the field of oncology, it is worth noting the ancient ways of treatment using products from nature which potentially can effectively support current therapies.

Review Methods. The literature review used PubMed, Google Scholar, Scopus, Science Direct, Frontiers, Medline, Bookshelf, and Elsevier databases, taking into consideration publications from the last eight years. However, the subject of research is niche, forcing the use of older papers.

Brief description of the state of knowledge. Plant extracts or their derivatives, tuberculin or sometimes mushrooms are most frequently employed in treating cancer. There are also publications on the anti-cancer properties of products from snail. Some researchers, however, believe there is little merit in turning to ancient methods. Extracts derived from snail bodies have been demonstrated to induce apoptosis in cancer cells, reduce their viability, and inhibit metastasis while exhibiting minimal or no detrimental impact on human cells. The interaction between snail hemolymph and anti-cancer drugs is sometimes synergistic. Snail organisms constitute specific micro-ecosystems that may contain micro-organisms. which, together with their metabolites, may also play an important role in immunotherapy. This problem, and the studies presented in the publications, must be verified by multiple methods.

Summary. The products extracted from the snail have the potential to be of significant importance in the future treatment of cancer patients. While the findings presented in various studies are valuable, they are insufficient for the reliable verification of treatment methods, as they are made mainly under *in vitro* conditions.

Key words

tumour, immunotherapy, anti-cancer therapy, snail

INTRODUCTION

Cancer is the second most frequently recorded cause of death in the world, including Poland, after circulatory failure [1]. Comparing the differences in the incidence of causes of death in men and women, it has been shown that the rate of increase in the incidence of cancer among men and women in recent years has been similar. In Poland, the highest incidence among women is cancer of the breast (22.8%), lungs (9.5%), and colon (9.0%). In contrast, among men, the incidence of prostate cancer (19.3%), lung cancer (17.5%), and colorectal cancer (11.5%) dominate. The leading cause of cancer deaths among both men and women, howevrer, is lung cancer [2]. The treatment of cancer patients routinely involves surgery, radiotherapy and/or chemotherapy, and immune stimulation. Despite some successes in oncology, it is impossible not to point out that the methods routinely used are very devastating to the body, and some types of cancer are resistant to them, forcing the search for new alternative treatments [3]. Gene therapy, ablative therapy, sonodynamic therapy, nanotechnology, and others receive much attention in research [4, 5].

The methods analyzed and implemented in treatment standards consider the general characteristics of tumour tissues. However, it is important to remember that tumours are diverse in structure and physiological characteristics. Currently, the search for standard methods of oncotherapy is based on some common features.

Tumours are not a homogeneous disease and exhibit different features that are distinct from healthy tissues, in the same way that cancer patients have diverse individual characteristics, heterogeneous psychophysical conditions, and physiological properties. Thus, the standards of treatment for different cancer patients must also be differentiated, and there is a need to search for such new treatment methods.

✉ Address for correspondence: Krzysztof Piotr Jasik, Department of Medical Sciences, Collegium Medicum, Jan Długosz University, Jerzego Waszyngtona, 42-200 Częstochowa, Poland
E-mail: k.jasik@ujd.edu.pl

Received: 18.10.2024; accepted: 11.06.2025; first published: 08.07.2025

THE FEATURES OF TUMOURS MOST COMMONLY CONSIDERED IN THE FORMULATION OF ONCOTHERAPY METHODS

Ability to induce and support angiogenesis. Tumour survival and growth depend on a constant supply of nutrients and oxygen. They also need to be able to remove metabolites and carbon dioxide. In this respect, tumours exhibit needs similar to those of healthy tissues. Even though angiogenesis in humans is very limited and involves wound healing, the reconstruction of the endometrium during the menstrual cycle, or perhaps the expansion of the collateral circulation, there is no ignoring the fact that cancer cells have a remarkable ability to induce angiogenesis [6]. Blood vessels in tumour tissue are generally atypical – excessively branched, larger in size, and exhibit a complex and irregular course and shape, which often leads to dissection and microhemorrhages. The activation of angiogenesis is caused by the disequilibrium of factors that balance this process, which either induce or inhibit angiogenesis. Thus, the extent of the angiogenesis is determined by the relationship between the angiogenic and anti-angiogenic factors. The best known inducer of angiogenesis is vascular endothelial growth factor A (VEGF-A), while the inhibitor is thrombospondin 1 (TSP-1) [7]. Some oncogenes and cells of the immune system, such as macrophages, neutrophils, and mast cells, can be involved in the induction of angiogenesis [8].

Angiogenesis inhibition seems to be an important component in anti-cancer therapy [9]. However, despite considerable literature on anti-angiogenic cancer therapies, they have been subjected to some criticism because, in clinical observations, these therapies have failed to result in health improvements, especially in cancers with strongly progressed tumours. In addition, cancers may become more invasive and accelerate metastasis as they develop resistance to anti-angiogenic therapy. It has been shown that inhibitors of VEGF and its receptors can promote invasive metastasis, in part through the creation of an increasingly hypoxic tumour microenvironment [10]. While anti-angiogenic activity is arguably important in oncotherapy, it may not be monotherapeutic [9].

Overall, oncology is looking for various factors, mainly isolated from plants, as well as organisms from other members of the living world, that have anti-proliferative and anti-angiogenic activity [11].

Avoiding dysplastic cell death. As mentioned above, the cancer cell survival rate of patients receiving treatment underlies the need to search for more effective cancer drugs. When physiological barriers to carcinogenesis are overcome, i.e. mutation of suppressor and mutator genes, further stages of the body's defence follow. The main protective force against malignant transformation is programmed cell death. The most frequent pathway for cancer cells to avoid death is the loss of TP53 function, and less commonly, decreased expression of pro-apoptotic factors and increased expression of apoptosis inhibitory factors, or an increase in the expression of survival factors. Also, autophagy, which involves the degradation of cell organelles in autophagosomes, is an important defence mechanism [12].

Paradoxically, since catabolites or intermediates formed during lytic processes can be used to feed and regenerate stressed cells, increased autophagy may have a cytoprotective effect by providing needed nutrients. It has also been shown that autophagy can induce not so much cell death as cell latency. In such a situation, the impact of epigenetic factors can lead to the resumption of the disease process after intense treatment. By analogy, necrosis could facilitate tumour progression by promoting angiogenesis and cell proliferation, as it releases pro-inflammatory signals, which causes immune-activated cells to migrate and induce inflammation [13].

Tumour progression by immune system inhibition. The prevailing hypothesis suggests that the immune system continuously monitors and regulates the activities of body cells and tissues. Consequently, most cells in the early stages of cancer transformation are identified and destroyed. Therefore, for neoplasmic changes to occur, intense carcinogenic conditions must exist, causing mutations in many cells. In addition, the immunosuppression promotes the progression of tumours. It is assumed that there is a correlation between weakened immunity in cancer patients, although at the same time, quite a few cancers are caused by viral infection. Thus it can be assumed that this is associated with increased virulence of oncogenic viruses. The results of studies on genetically modified mice with a deficiency of specific elements of the immune system showed that in such mice induced tumours developed faster than in animals without genetic modification. In particular, deficiencies in the function and presence of CD8+ cytotoxic T cells, Th1CD4+ accessory lymphocytes and NK cells, promoted neoplasmic processes. In addition, a tendency towards neoplastic lesions has been described in transplant mice without genetic knockout, only with iatrogenic immunosuppression [14].

Also, a high risk of cancer has been observed in humans after transplantation due to the need to use immunosuppression [15]. It is likely that the cancer cells were originally formed in the donor. Due to an efficient immune system, they would be destroyed, but since the recipient must be immunosuppressed, the cancer cells could survive and undergo progression.

In some human cancers, such as colorectal or ovarian cancers, it has been observed that within a tumour lesion, a lymphocyte infiltrate may appear. In such cases, a better prognosis is associated with the presence of NK cells than in those instances where such an infiltrate is not found [16]. In addition, it has been proven that tumour cells can secrete TGF-β and other immunosuppressive factors that inhibit NK cells and cytotoxic lymphocytes [14].

Alteration of the metabolism of cancer cells. The intense, uncontrolled proliferation of cancer cells requires a corresponding change in metabolism. Normal cells under aerobic conditions convert glucose to pyruvate in the cytosol and eventually to carbon dioxide and water in the mitochondria. This results in a considerable energy benefit. Otto Warburg in the 1930s observed a re-programming of the metabolic processes of cancer cells in the normal presence of oxygen. This process was originally referred to as oxygen glycolysis, but today the phenomenon is called the Warburg effect. Considering fundamental biochemical knowledge, this mechanism seems incoherent, because cancer cells must recompense for the 18 times lower ATP production efficiency, compared to oxidative phosphorylation. Nevertheless, this process deserves attention in the search for oncology therapies [17, 18]. The regulation of GLUT-1 glucose transporters to

increase glucose import into the cell's cytoplasm is probably partially responsible for this. The process of increased glucose uptake and metabolic conversion by cancer cells has been demonstrated using positron emission tomography (PET). Over-expression of GLUT-1 on cell membrane was observed in greater biological aggressiveness of thyroid cancer, being found more often in anaplastic thyroid cancers than in well-differentiated forms [19].

Although the Warburg effect has been known for 100 years, many unexplained problems remain regarding the phenomenon.

Alternative treatments used today. Related to the subject of this review, plant extracts or their derivatives are most often used in oncology therapies [20, 21]. Natural factors also used in oncology treatment include *Mycobacterium tuberculosis* and *M. bovis* metabolites [22] or products extracted from mushrooms [23]. Products derived from other organisms of different taxonomic groups receive much less attention in oncology [24].

Utilising ancient methods of treatment which to date are unsubstantiated scientifically, to some seems useless. Nevertheless, it is worth studying these methods as it may turn out that their use may have application value. There are research papers that prove the great medical potential of pharmaceuticals extracted from invertebrates. Among invertebrate organisms, Gastropoda seems to be very interesting. In some cases, products extracted from Mollusca, one of the most abundant groups of animals on earth, are already used in pharmacotherapy.

Mollusca colonize aquatic and terrestrial environments, and include bivalves, snails, and cephalopods, whose culinary values are used in several cultures. Snails (Gastropoda) include nearly 65,000 species known so far, living in seawater, freshwater, or on land. A considerable number of gastropods are species that possess a sizable shell. Anatomically, the structure of the snail is composed of three basic elements: the head, legs, and visceral sacs [25]. The characteristic spiral body structure of snails is due to interesting, complex developmental mechanisms [26, 27].

The extraction of bioactive factors from snails has been a practice for centuries, resulting in products with diverse therapeutic effects. Scientific literature exists on the anti-cancer properties of snail products [28, 29]. Novel treatment methods are founded on the properties of tumours as tissues and their complexes, physiologically and morphologically distinct from normal tissues. The study of these features is of significant importance in the search for new alternative treatments [30].

The aim of this literature review is to evaluate the possible anti-cancer properties of snail extracts and the products derived from them.

REVIEW METHODS

The literature review used PubMed, Google Scholar, Scopus, Science Direct, Frontiers, Medline, Bookshelf, and Elsevier databases. Key words searched for were: unconventional methods in oncology, extracted from snails – mucus, hemolymph, shells, extract, caviar – in combination with the phrase anti-cancer/anti-tumour. The review took into consideration publications from the last eight years. However, the subject matter is niche and forces the use of older papers. Data described in non-reviewed sources were rejected. It is essential to note that publications that merely reiterated existing content, as well as those that, according to the authors, did not provide relevant information, were also excluded from the initial set of literature.

The presented literature review encompasses information published in English.

The process of selecting the literature included in the review, along with the decisions made at various stages of the review, is presented using a PRISMA flowchart (Fig. 1).

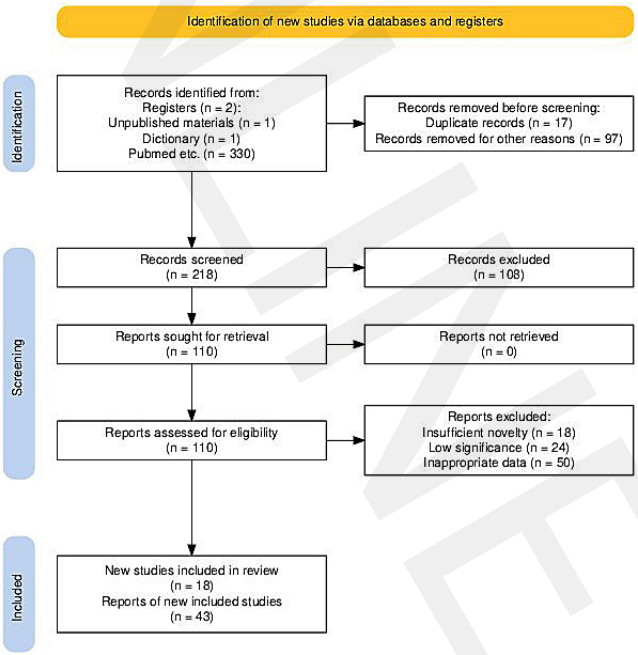

Figure 1. Flowchart diagram of the literature review process

DESCRIPTION OF THE STATE OF KNOWLEDGE

Hemolymph. Hemolymph is composed of a complex mixture of bioactive components in the form of peptide glycans, glycopeptides, and proteins, compounds which are active biochemically as well as pharmacologically. Glycoproteins and peptides with antimicrobial activity are important components in innate immunity. Metalloproteins contained in hemolymph exhibit immunostimulatory and antitumour effects. Carbohydrate groups in hemocyanin are responsible for the high ability to raise immune activity. In several studies, treating cells with hemocyanin increased the humoral anti-tumour response and inhibited tumour growth and metastasis to nearby tissues and organs [28, 30, 31]. Adding the described extract to pharmaceutical, and cosmetic products has a stimulating effect on regeneration and wound healing [31].

Hemocyanins in the hemolymph of *Helix lucorum* and *Rapana venosa* cause a decrease in the viability of bladder cancer cells. Gene expression studies showed increased expression of genes responsible for apoptosis and activation of the immune system [32].

Chiumiento et al. showed that hemocyanin obtained from *Pomacea canaliculata* not only induces a pro-inflammatory

effect on the macrophage cell line THP-1 (Tohoku Hospital Paediatrics-1) by increasing levels of IL1-β and TNF-α, as well as promoting phenotypic changes associated with the differentiation of monocytes into macrophages. In addition, *Pomacea canaliculata* and keyhole limpet hemocyanins were observed to induce the same humoral response in mice. This represents a promising immunostimulatory property for oncotherapy, especially since marine snail keyhole limpet has been extensively studied and successfully used as a non-specific immuno-stimulant in the treatment of bladder cancer [33].

It has been reported that hemocyanins isolated from the hemolymph of snails *H. aspersa*, *H. lucorum,* and *R. venosa,* significantly reduced the viability of cells of the HT-29 line [28]. In this case, studies based on microscopic and submicroscopic analyses and MTT survival assays provided a basis for reasonable conclusions about the effectiveness of the formulations.

The effects of hemolymph on the cells studied can be diverse, such as the inhibition of the cell cycle, reduction of nutrient supply and metabolite removal, and induction of cell death. The isolated hemocyanin subunits RvH1 and RvH2, derived from the snails *H. pomatia* and *R. thomasiana*, respectively, have been observed to elicit disparate outcomes. This phenomenon was observed *in vitro* using breast cancer cell lines – MDA-MB-231, MDA-MB-468, BT-474, BT-549, SK-BR-3, and MCF-7. It has also been noted that hemolymph taken from the mentioned species enhances the effect of cisplatin [34]. At the same time, the examined factors were shown to be less toxic to the normal human breast cells MCF-10A.

Hemocyanins from *Concholepas concholepas* and *Fissurella latimarginata* are safe and useful carbohydrate mimotope transporters, and therefore new equivalents for increasing peptide immunogenicity potentially important in cancer vaccine research [35]. In addition to treating cancer patients, the immunostimulatory properties of snail hemocyanins can be used in cases of viral infections. For example, the RVH2-E unit of *R. venosa* hemolymph has demonstrated anti-viral activity against the herpes simplex virus type 1 (HSV-1) [36].

Lectins found in the mucus or hemolymph of snails deserve separate attention. Despite a considerable number of literature data suggesting the negative effects of lectins on the human body, there is a clear contradiction to these data. A significant number of authors of publications have noted that glycans, through their diverse polysaccharide structures, can enhance a myriad of cell signaling pathways involved in development, growth, immuno-communication, and viability. Research into the immunostimulatory properties of glycoproteins extracted from molluscs provides information on additional possible applications [37, 38].

Currently, *Helix pomatia* lectin, which recognizes O-GlcNAc residues in metastatic breast cancer, and *H. aspersa* lectin, which recognizes O-GalNAc on various tumour cells, are used in oncology diagnostics [37, 38].

In addition, it was found that some lectins did not exhibit anti-cancer activity; however, most inhibited cell proliferation, caused cell cycle arrest, and induced apoptosis through the regulation of intrinsic and extrinsic pathways. Moreover, immunomodulatory mechanisms were also identified and considered a valuable resource for cancer treatment. The anti-cancer effect of hemocyanin has also been confirmed *in vivo* for colon cancer in mice. As in *Mycobacterium bovis*, it induces a cascade of immune processes that inhibit tumour growth and metastasis [39, 40]. The authors suggest that this action may be effective in other types of cancer. It is noteworthy that this is one of the few studies on the anti-cancer effects of hemocyanins in broader aspects than *in vitro* studies, which translates into survival analysis of organisms, which is part of preclinical research.

Mucus. Snails produce different types of mucus, containing a variety of substances that affect their functions. The mucus of the leg has a watery consistency as it contains about 96–97% water and limosin. This type of mucus is mainly used for the movement of the snail. Cryptosin is a type of secretion produced all over the body; its consistency is much denser and viscous. It has been proven that stressful situations induce the production of this secretion. The types of mucus mentioned above have hygroscopic properties [41].

The composition of these secretions is a mixture of proteoglycans, glycosaminoglycans (GAGs), glycoprotein enzymes, hyaluronic acid, copper peptides, antimicrobial peptides (AMPs) and metal ions, such as Zn, Fe, Cu, Mn, and Se. Studies have shown that the secretion exhibits a variety of biological activities: anti-microbial, anti-oxidant, anti-tyrosinase, and anti-cancer [42, 43].

Studies of Hep2G and Caco2 which had cell lines in a medium supplemented with *E. desertorum* snail mucus extract, showed increased expression of anti-oxidants (catalase, SOD, GSH, among others) in the cells. The expression of GSTA1, catalase, SOD, GPx, and suppressor genes (*p53*, *Rb*, *APC*, and *PTEN*) was also increased [44].

Treatment of the cervical cancer cell line HeLa with *Achatina fulica* mucus with the addition of silver nanoparticles, inhibited these cells. The growth inhibition effect of the cells tested was directly proportional to the concentration of mucus [45]. The growth inhibition effect and induction of apoptosis of melanoma cells (SK-MEL-28 and IGR-39 lines) under the influence of *Helix aspersa* mucus were also observed *in vitro* [46]. Studies on the effects of *Helix aspersa* maxima mucus on the expression of MMP2, a protein involved in metagenesis, showed that MMP2 expression is only slightly decreased in SK-MEL-28 cells, but significantly decreased in the IGR-39 line. This extract blocked the adhesion of IGR-39 cells by inhibiting the function of integrins $\alpha_2\beta_1$ (45%) and $\alpha_v\beta_3$ (38%), and by reducing the expression of integrins α_v and β_1 [47].

A similar study was also performed using mucus from other snail species. The mucus from *Limax maximus* and *Arion rufus* reduced the metabolic activity of human keratinocytes (CCD 1106 KERTr) and melanoma cells (A-375), and also reduced cell proliferation in both cell lines tested. It can therefore be concluded that the mucus of these snails shows anti-cancer potential [47]. *H. aspersa* mucus reduces the cell viability of the HT-29 line [32, 48]. Mucus fractions of the snail *Achatina fulica* reduce the viability of cells of the mammary cancer line MCF-7, and had the same effect on kidney cells of the Vero line [47].

All of the snail mucus components may significantly affect the development and survival of cancer cells [39]. It is interesting that a positive effect of non-lyophilized mucus on human dermal fibroblasts of the NHDF lineage was observed [49, 50].

Caviar (snail eggs). Snail eggs have a milky colour, are opaque, and are surrounded by a light-clear delicate shell. The size of a single egg is about 3–6 mm in diameter, and weigh 3–6 grams. Lyophilized snail germ extract has active substances in its composition, such as:

- proteins and phospholipids;
- vitamins A, D, and E, as well as B vitamins;
- elements P, Zn, Mg and Si;
- unsaturated fatty acids.

Analysis of the chemical composition of the embryos of the large garden snail showed the following: water – 84.5%, carbohydrates – 6.7%, ash – 5.0%, protein – 3.7%, lipids – 0.1%. However, the species, food, breeding conditions, and age of snails, affect the differences in the chemical components of the eggs [51, 52]. Various components of white caviar show bioactive effects on different cells [53].

According to the study by Matusiewicz et al., treatment of *H. aspersa* aspersa and *H. aspersa* maxima extracts from eggs for 24h led to a decrease in the survival rate of cells of the CACO-2 line, compared to cells treated with deionized water. Such an effect was not observed after treating the cells for 72h. Treatment with egg extract for 24 also damaged the cell membranes of the CACO-2 line. However, treatment for 72h did not affect the secretion of LDH (a marker of cell membrane breakdown). Egg extracts also induced apoptosis and reduced the frequency of necrosis in the cells tested. Such abundant results were obtained using MTT colorimetric methods, measuring lactate dehydrogenase activity and determining the type of cell death by flow cytometry [51]. The limiting effect of snail caviar on SCC-25 cells was also noted *in vitro* conditions [50]. These studies raise the hope that white caviar could be used to treat and even prevent cancer.

Shells. In ancient times, mollusk shells were used in many medical and paramedical applications. The effect of snail shell powder on wound healing was observed *in vivo* studies in mice; the powder accelerated wound healing, stimulated angiogenesis, and showed anti-inflammatory effects. The anti-inflammatory activity of the shells and regulation of the inflammatory process may be important in cancer treatment, as inflammation and wound healing show many consistent mechanisms [54].

Studies of the properties of the powder obtained from the shells of various snail species showed their anti-oxidant properties. The effect of the shell on the Caco-2 cancer cell line was also analyzed, and it was found that although the anti-oxidant activity of the shell extract was higher than that of other parts of the snail, the shell extract did not show a significant reduction in the viability of the cancer cell line. The observed result may be attributed to the presence of iron in the analyzed substrate [29]. Studies have demonstrated that the *Conus geographus* shell extract exerts a growth inhibitory effect on the cells of breast cancer (MCF-7), human epithelial breast cancer (MDA-MB-231), ovarian cancer (SKOV-3), and hepatocellular carcinoma (HepG2) cancer lines. The findings revealed that the *C. geographus* shell extract exerts a comparable inhibitory effect on SKOV-3 cells to that of cisplatin [55].

Extracts of snail body. Among the various studies on the pharmacological potential of snail-derived materials, analyses of the effects of snail body extracts on various normal and tumour-transformed cells are also relevant.

The extract from the snail *Helix aspersa* induces apoptosis in appropriate concentrations and necrosis in others, but unequivocally causes cell death in the Hs578T line. This extract also increases the expression of *TNF-α* genes and decreases the expression of NK-κB. On the other hand, the extract has been shown to reduce the expression of the *p53* and PTEN genes [56].

The crude extract of *Euchelus asper* was evaluated for anticancer activity. The methanolic extract of *E. asper* was found to have anti-angiogenic activity *in ovo* (in feotal membranes of birds) and anti-proliferative activity *in vitro* on A549 lung cancer cells [57]. Diverse methodologies using, e.g., histological, cytotoxic (SRB), scratch wound healing, and cell cycle analysis by flow cytometry. The tested extract also effectively inhibited the proliferation of lung cancer cells by reducing the expression of MMP-2/9. The potential anti-angiogenic ability of the methanolic extract of *Meretrix casta*, *M. meretrix*, *Telescopium telescopium,* and *Bursa crumena*, was demonstrated, suggesting a supressive effect on tumour metastasis [58].

SUMMARY

Each patient presents individual characteristics due to age, physiological condition, physical activity, etc., therefore, the treatment of any disease has to be multi-dimensional. The same is also true for oncological diseases. In addition, cancers are very heterogeneous. Each patient requires different treatments depending on the type of cancer, its location, and propensity to metastise.

In principle, the goal of oncology therapy should be the destruction of cancer cells with minimal damage to healthy cells and organs.

Considering the differences between patients and cancer types, there is a need to search for new factors that enable targeted therapy [59].

Snail extracts appear to have an activity that meets the above conditions. They exhibit a broad spectrum of biological activity, which further increases the therapeutic potential for cancer treatment. Snail body extracts induce apoptosis of cancer cells, reduce their viability, have an anti-proliferative effect, and inhibit metastasis, with little or no damage to human cells. It is impossible to overlook the regenerative properties of snail products. Snail hemolymph interacts synergistically with drugs used in anti-cancer therapy, giving hope for its use in clinical trials. Despite the results obtained, however, it should be remembered that most of the studies conducted were *in vitro*, so the actual effect may be different in clinical settings.

An important problem in the study of mucus properties is that it is very labile and its physicochemical properties change rapidly over time from the moment of secretion. It would therefore be necessary to consider whether the sterilization and freeze-drying process is sensible in the creation of formulations.

Snails that live in the wild maintain a specific microbiome and microbiota in their bodies. It has been shown that the various surface and internal spaces of snails constitute specific micro-ecosystems that may contain microorganisms atypical of the human physiological microflora. Of the dominant bacteria, several are known for their ability to metabolize

complex polysaccharides (e.g. *Rhizobium* spp., *Shewanella* spp., *Pedobacter* spp., *Acinetobacter* spp., and *Alcaligenes* spp.) [60]. These microorganisms and their metabolites may also play an important role in cancer immunotherapy [61]. This forces the verification effects of studies using freeze-dried or sterilized materials derived from snails.

Unlike mucus, hemolymph and caviar do not need to be chemically processed.

Among the described anti-cancer factors obtained from snails, there remain quite a few unknowns. For example, it has been pointed out that the proportions of essential components may not be irrelevant. It has even been suggested that a specific proportion of certain amino acids commonly found in mollusks, such as Gly, Leu, Ile and Val, may be important in oncotherapy [43]. It is also important to note that any physicochemical interference during the extraction of the test material from the snails may result in an alteration of the established quantitative and qualitative relationships.

In conclusion, the products extracted from snails could be of significant importance in treating cancer patients in the future. It should be noted, however, that a significant proportion of the studies presented in this review were based on in vitro methods. *In vivo*, studies are needed to assess the potential of Gastropod-derived substrates for new oncological treatments.

There is a big difference in observing the effects of snail-derived substances on selected biological processes and in their medical applications. The current state of knowledge does not allow us to determine the possibility of developing oncological treatments using snail products. However, there is substantial literature indicating an interest in using such products in oncotherapy. Therefore It is worth noting that studies on obtaining specific drugs or treatments should also take into account many of the above-mentioned aspects.

REFERENCES

1. Burzyńska M, Pikala M. Changes in mortality of Polish residents in the early and late old age due to main causes of death from 2000 to 2019. Front Public Health. 2023;11:1060028. https://doi.org/10.3389/fpubh.2023.1060028
2. Didkowska J, Wojciechowska U, Michalek IM, et al. Cancer incidence and mortality in Poland in 2019. Sci Rep. 2022;12(1):10875. https://doi.org/10.1038/s41598-022-14779-6
3. Huang L, Yang C, Chen Y, et al. CRISPR-Mediated Base Editing: Promises and Challenges for a Viable Oncotherapy Strategy. Hum Gene Ther. 2023;34(15–16):669–681. https://doi.org/10.1089/hum.2023.045
4. Debela DT, Muzazu SG, Heraro KD, et al. New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Med. 2021;9:20503121211034366. https://doi.org/10.1177/20503121211034366
5. Krasteva N, Georgieva M. Promising Therapeutic Strategies for Colorectal Cancer Treatment Based on Nanomaterials. Pharmaceutics. 2022;14(6):1213. https://doi.org/10.3390/pharmaceutics14061213
6. Lugano R, Ramachandran M, Dimberg A. Tumour angiogenesis: causes, consequences, challenges and opportunities. Cell Mol Life Sci. 2020;77(9):1745–1770. https://doi.org/10.1007/s00018-019-03351-7
7. Petrik J, Lauks S, Garlisi B, et al. Thrombospondins in the tumour microenvironment. Semin Cell Dev Biol. 2024;155(Pt B):3–11. https://doi.org/10.1016/j.semcdb.2023.05.010
8. Xu X, Lai Y, Hua ZC. Apoptosis and apoptotic body: disease message and therapeutic target potentials. Biosci Rep. 2019;39(1):BSR20180992. https://doi.org/10.1042/BSR20180992
9. Lopes-Coelho F, Martins F, Pereira SA, et al. Anti-Angiogenic Therapy: Current Challenges and Future Perspectives. Int J Mol Sci. 2021;22(7):3765. https://doi.org/10.3390/ijms22073765
10. Muz B, de la Puente P, Azab F, et al. The role of hypoxia in cancer progression, angiogenesis, metastasis, and resistance to therapy. Hypoxia (Auckl). 2015;3:83–92. http://dx.doi.org/10.2147/HP.S93413.
11. Ciavatta ML, Lefranc F, Carbone M, et al. Marine Mollusk-Derived Agents with Antiproliferative Activity as Promising Anticancer Agents to Overcome Chemotherapy Resistance. Med Res Rev. 2017;37(4):702–801. https://doi.org/10.1002/med.21423
12. Vitale I, Pietrocola F, Guilbaud E, et al. Apoptotic cell death in disease-Current understanding of the NCCD 2023. Cell Death Differ. 2023;30(5):1097–1154. https://doi.org/10.1038/s41418-023-01153-w
13. Peng P, Lou Y, Wang J, et al. Th1-Dominant CD4+T Cells Orchestrate Endogenous Systematic Antitumour Immune Memory After Cryo-Thermal Therapy. Front Immunol. 2022;13:944115. https://doi.org/10.3389/fimmu.2022.944115
14. Zwart ES, Yüksel E, Pannekoek A, et al. De Novo Carcinoma after Solid Organ Transplantation to Give Insight into Carcinogenesis in General-A Systematic Review and Meta-Analysis. Cancers (Basel). 2021;13(5):1122. https://doi.org/10.3390/cancers13051122
15. Friman TK, Jäämaa-Holmberg S, Åberg F, et al. Cancer risk and mortality after solid organ transplantation: A population-based 30-year cohort study in Finland. Int J Cancer. 2022;150(11):1779–1791. https://doi.org/10.1002/ijc.33934
16. Nersesian S, Schwartz SL, Grantham SR, et al. NK cell infiltration is associated with improved overall survival in solid cancers: A systematic review and meta-analysis. Transl Oncol. 2021;14(1):100930. https://doi.org/10.1016/j.tranon.2020.100930
17. Tran Q, Lee H, Kim C, et al. Revisiting the Warburg Effect: Diet-Based Strategies for Cancer Prevention. Biomed Res Int. 2020;2020:8105735. https://doi.org/10.1155/2020/8105735
18. DeBerardinis RJ, Chandel NS. We need to talk about the Warburg effect. Nat Metab. 2020;2(2):127–129. https://doi.org/10.1038/s42255-020-0172-2
19. Heydarzadeh S, Moshtaghie AA, Daneshpour M, et al. Correction to: Regulators of glucose uptake in thyroid cancer cell lines. Cell Commun Signal. 2022;20(1):11. https://doi.org/10.1186/s12964-020-00586-x
20. Thronicke A, Schad F, Debus M, et al. Viscum album L. Therapy in Oncology: An Update on Current Evidence. Viscum album L. Therapie in der Onkologie: Ein Update zur bestehenden Evidenz. Complement Med Res. 2022;29(4):362–368. https://doi.org/10.1159/000524184
21. Wang X, Chan YS, Wong K, et al. Mechanism-Driven and Clinically Focused Development of Botanical Foods as Multitarget Anticancer Medicine: Collective Perspectives and Insights from Preclinical Studies, IND Applications and Early-Phase Clinical Trials. Cancers (Basel). 2023;15(3):701. https://doi.org/10.3390/cancers15030701
22. Duan H, Xia W, Xu D, et al. Peripheral tuberculin purified protein derivative specific T cell immunoreactivity dynamics in non-muscle invasive bladder cancer patients receiving bacillus Calmette-Guerin instillation treatment. Front Oncol. 2022;12:927410. https://doi.org/10.3389/fonc.2022.927410
23. Fonseca J, Vaz JA, Ricardo S. The Potential of Mushroom Extracts to Improve Chemotherapy Efficacy in Cancer Cells: A Systematic Review. Cells. 2024;13(6):510. https://doi.org/10.3390/cells13060510
24. Wali AF, Majid S, Rasool S, et al. Natural products against cancer: Review on phytochemicals from marine sources in preventing cancer. Saudi Pharm J. 2019;27(6):767–777. https://doi.org/10.1016/j.jsps.2019.04.013
25. Solem GA. "gastropod." Encyclopedia Britannica, September 3, 2024. Online https://www.britannica.com/animal/gastropod.
26. Johnson AB, Fogel NS, Lambert JD. Growth and morphogenesis of the gastropod shell. Proc Natl Acad Sci U S A. 2019;116(14):6878–6883. https://doi.org/10.1073/pnas.1816089116
27. Namigai EKO, Shimeld SM. Live Imaging of Cleavage Variability and Vesicle Flow Dynamics in Dextral and Sinistral Spiralian Embryos. Zoolog Sci. 2019;36(1):5–16. https://doi.org/10.2108/zs180088
28. Georgieva A, Todorova K, Iliev I, et al. Assessment of the In Vitro and In Vivo Antitumour Activity of Hemocyanins from Helix aspersa, Helix lucorum, and Rapana venosa in a Graffi Myeloid Tumour Model. Biomedicines. 2023;11(6):1545. https://doi.org/10.3390/biomedicines11061545
29. Rompas JJI, Laatung S, Gunawan WB, et al. Rice field snail shell anticancer properties: An exploration opinion. Front Oncol. 2023;12:1078981. https://doi.org/10.3389/fonc.2022.1078981
30. Frost HR. Analyzing cancer gene expression data through the lens of normal tissue-specificity. PLoS Comput Biol. 2021;17(6):e1009085. https://doi.org/10.1371/journal.pcbi.1009085
31. Deng T, Gao D, Song X, et al. A natural biological adhesive from snail mucus for wound repair. Nat Commun. 2023;14(1):396. https://doi.org/10.1038/s41467-023-35907-4
32. Georgieva A, Todorova K, Iliev I, et al. Hemocyanins from Helix and Rapana Snails Exhibit in Vitro Antitumour Effects in Human

Colorectal Adenocarcinoma. Biomedicines. 2020;8(7):194. https://doi.org/10.3390/biomedicines8070194
33. Chiumiento IR, Tricerri MA, Cortéz MF, et al. Pomacea canaliculate hemocyanin as a novel natural immunostimulant in mammals. Front Immunol. 2025;15:1490260. https://doi.org/10.3389/fimmu.2024.1490260
34. Petrova M, Vlahova Z, Schröder M, et al. Antitumour Activity of Bioactive Compounds from Rapana venosa against Human Breast Cell Lines. Pharmaceuticals (Basel). 2023;16(2):181. https://doi.org/10.3390/ph16020181
35. Palacios M, Tampe R, Del Campo M, et al. Antitumour activity and carrier properties of novel hemocyanins coupled to a mimotope of GD2 ganglioside. Eur J Med Chem. 2018;150:74–86. https://doi.org/10.1016/j.ejmech.2018.02.082
36. Dolashka P, Daskalova A, Dolashki A, et al. De Novo Structural Determination of the Oligosaccharide Structure of Hemocyanins from Molluscs. Biomolecules. 2020;10(11):1470. https://doi.org/10.3390/biom10111470
37. Pietrzyk AJ, Bujacz A, Mak P, et al. Structural studies of Helix aspersa agglutinin complexed with GalNAc: A lectin that serves as a diagnostic tool. Int J Biol Macromol. 2015;81:1059–1068. https://doi.org/10.1016/j.ijbiomac.2015.09.044
38. Muñoz SM, Vallejos-Baccelliere G, Manubens A, et al. Structural insights into a functional unit from an immunogenic mollusk hemocyanin. Structure. 2024;32(6):812–823.e4. https://doi.org/10.1016/j.str.2024.02.018
39. Gesheva V, Chausheva S, Mihaylova N, et al. Anti-cancer properties of gastropodan hemocyanins in murine model of colon carcinoma. BMC Immunol. 2014;15:34. https://doi.org/10.1186/s12865-014-0034-3
40. Mukherjee N, Julián E, Torrelles JB, et al. Effects of Mycobacterium bovis Calmette et Guérin (BCG) in oncotherapy: Bladder cancer and beyond. Vaccine. 2021;39(50):7332–7340. https://doi.org/10.1016/j.vaccine.2021.09.053
41. Wargala E, Zalewska A, Sławska M, et al. Snail mucus as an innovative ingredient used in the cosmetology and medical industry. Aesth Cosmetol Med. 2023;12(2):45–49. https://doi.org/10.52336/acm.2023.001
42. Kandeil MA, Mona MM. Evaluation of antioxidant, antityrosinase, and anticancer activity of mucus extract from both Egyptian land snails, Eremina desertorum and Helix aspersa, with emphasis on their chemical profiles. J Exp Zool A Ecol Integr Physiol. 2024;341(2):182–192. https://doi.org/10.1002/jez.2773
43. Matusiewicz M, Kosieradzka I, Niemiec T, et al. In Vitro Influence of Extracts from Snail Helix aspersa Müller on the Colon Cancer Cell Line Caco-2. Int J Mol Sci. 2018;19(4):1064. https://doi.org/10.3390/ijms19041064
44. Atta SA, Ibrahim AM, Megahed FAK. In-Vitro Anticancer and Antioxidant Activities of Eremina desertorum (Forsskal, 1775) Snail Mucin. Asian Pac J Cancer Prev. 2021;22(11):3467–3474. https://doi.org/10.31557/APJCP.2021.22.11.3467
45. Mane PC, Sayyed SAR, Kadam DD, et al. Terrestrial snail-mucus mediated green synthesis of silver nanoparticles and in vitro investigations on their antimicrobial and anticancer activities. Sci Rep. 2021;11(1):13068. https://doi.org/10.1038/s41598-021-92478-4
46. Ellijimi C, Ben Hammouda M, Othman H, et al. Helix aspersa maxima mucus exhibits antimelanogenic and antitumoural effects against melanoma cells. Biomed Pharmacother. 2018;101:871–880. https://doi.org/10.1016/j.biopha.2018.03.020
47. Leśków A, Tarnowska M, Szczuka I, et al. The effect of biologically active compounds in the mucus of slugs Limax maximus and Arion rufus on human skin cells. Sci Rep. 2021;11(1):18660. https://doi.org/10.1038/s41598-021-98183-6
48. Devan E, Maduraiveeran H, Raja K, et al. Antitumour activity of edible fishes (Channa striata and Anabas testudineus) and gastropods (Helix aspersa and Pila virens) rudimentary mucus against HT-29 cell line and its biochemical properties. JoBAZ 2025;86, 2. https://doi.org/10.1186/s41936-024-00423-4
49. Waluga-Kozłowska E, Jasik K, Wcisło-Dziadecka D, et al. Snail mucus-a natural origin substance with potential use in medicine. Acta Pol Pharm. 2021;78(6):793–800. https://doi.org/10.32383/appdr/145377
50. Unpublished data: In vitro analysis of the influence of Cornu aspersum aspersum snail embryo homogenate on normal cells and tongue cancer cells. https://ppm.sum.edu.pl/info/phd/SUMc3fe7b78771e4f4cb29a5185dfd36913/
51. Matusiewicz M, Marczak K, Kwiecińska B, et al. Effect of extracts from eggs of Helix aspersa maxima and Helix aspersa aspersa snails on Caco-2 colon cancer cells. Peer J. 2022;10:e13217. https://doi.org/10.7717/peerj.13217
52. Maćkowiak-Dryka M, Szkucik K, Pyz-Łukasik R. Snail Eggs as a Raw Material for the Production of a Caviar Substitute. J Vet Res. 2020;64(4):543–547. https://doi.org/10.2478/jvetres-2020-0062
53. Herman A, Wińska P, Białek M, et al. Biological Properties of the Mucus and Eggs of Helix aspersa Müller as a Potential Cosmetic and Pharmaceutical Raw Material: A Preliminary Study. Int J Mol Sci. 2024;25(18):9958. https://doi.org/10.3390/ijms25189958
54. Andrade PHM, Portugal LC, Rondon ES, et al. Effect of powdered shells treatment of the snail Megalobulimus lopesi on wounds of diabetic rats. Acta Cir Bras. 2018;33(2):185–196. https://doi.org/10.1590/s0102-865020180020000010
55. Alburae NA, Mohammed AE. Antiproliferative effect of the Red Sea cone snail, Conus geographus. Trop J Pharm Res. 2020;19(3):577–581. http://dx.doi.org/10.4314/tjpr.v19i3.17.)
56. El Ouar I, Braicu C, Naimi D, et al. Effect of Helix aspersa extract on TNFα, NF-κB and some tumour suppressor genes in breast cancer cell line Hs578T. Pharmacogn Mag. 2017;13(50):281–285. https://doi.org/10.4103/0973-1296.204618
57. Agrawal S, Chaugule S, More S, et al. Methanolic extract of Euchelus asper exhibits in-ovo anti-angiogenic and in vitro anti-proliferative activities. Biol Res. 2017;50(1):41. https://doi.org/10.1186/s40659-017-0147-2
58. Gupta P, Arumugam M, Azad RV, et al. Screening of antiangiogenic potential of twenty two marine invertebrate extracts of phylum Mollusca from South East Coast of India. Asian Pac J Trop Biomed. 2014;4(Suppl 1):S129–S138. https://doi.org/10.12980/APJTB.4.2014C701
59. Shuel SL. Targeted cancer therapies: Clinical pearls for primary care. Can Fam Physician. 2022;68(7):515–518. https://doi.org/10.46747/cfp.6807515
60. Belouhova M, Daskalova E, Yotinov I, et al. Microbial diversity of garden snail mucus. Microbiologyopen. 2022;11(1):e1263. https://doi.org/10.1002/mbo3.1263
61. Huang J, Liu W, Kang W, et al. Effects of microbiota on anticancer drugs: Current knowledge and potential applications. EBioMedicine. 2022;83:104197. https://doi.org/10.1016/j.ebiom.2022.104197