

Natural Product for drug delivery

Natural Product and Its Nanoparticles for Cancer Treatment

Kadriye Ozlem Saygi

Department of Chemistry, Faculty of Arts and Sciences, Vocational School, Tokat Gaziosmanpasa University, 60250 Tokat, Turkey.

Abstract: Growing interest in natural anticancer therapies has been noted in recent decades, primarily as a result of unresolved medication resistance issues. Many *invitro* and *invivo* studies have shown how natural chemicals can inhibit tumour growth by affecting various cellular processes and signalling pathways. By improving the bioavailability and in vivo stability, lowering side effects, and enhancing target-specific activity may significantly improve their anticancer efficacy. The research works that relate to nanostructured systems with natural substances for innovative drug delivery methods in anticancer therapy will be the main emphasis of this review. These systems have the potential to overcome many of the limitations of traditional drug delivery methods, such as poor solubility and stability, low bioavailability, and variable pharmacokinetics. They can also give specific delivery of the affected area while minimizing the side effects. Therefore, it is essential to recognize the possibilities of nanostructured medication delivery methods to provide some safe and effective cancer-treatment for patients. Nanostructured medication delivery methods for natural products can improve drug solubility, bioavailability, and consistency, and also provide controlled and targeted the drug's release to the affected area. This would reduce the amount of drug needed, making it more cost-effective, and decrease the side effects of the drugs. As such, these systems could provide a more effective treatment for cancer patients. Nanostructured drug delivery systems could revolutionize the way cancer is treated, and improve patient outcomes. Furthermore, such systems could be used in other applications, such as targeted release of other therapeutic agents.

Keywords: Natural products: drug discovery: drug delivery systems, nanoparticles

*Corresponding Author

Kadriye Ozlem Saygi , Department of Chemistry, Faculty of Arts and Sciences, Vocational School, Tokat Gaziosmanpasa University, 60250 Tokat, Turkey.

Received On 22 October, 2022 Revised On 9 January, 2023 Accepted On 8 February, 2023 Published On 13 March, 2023

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation Kadriye Ozlem Saygi , Natural Product Drug Delivery Methods for Oncology.(2023).Int. J. Trends in OncoSci.I(I), I-7

CC (1) (S) (E)

I. INTRODUCTION

One of the main causes of death in the globe is cancer¹. It is estimated that 23.6 million new cancer cases will occur annually by 2030². This indicates a dire need for better cancer treatments and prevention strategies to prevent the further spread of this deadly disease. Female breast cancer (523,000 instances), colorectal cancer (500,000), lung cancer (470,000), and prostate cancer were the most frequent cancer locations (450,000). With almost 1.4 million new cases each year, prostate cancer is the second most frequent disease in men and the fourth most common cancer overall in 2020. These four cancers represent half of the overall burden of cancer in Europe. Lung (388,000 fatalities), colorectal (243,000), breast (138,000), and pancreatitis were the leading causes of mortality. Despite this, prevention and early detection initiatives have the potential to reduce mortality from these four cancers significantly. This is likely since the prevalence of smoking, unhealthy diets, and other lifestyle factors that are known increasing the risk of developing these cancers. Additionally, certain genetic factors may additionally take a role in the evolution of these cancers. These cancers account for a large portion of all cancer cases and deaths in Europe, showing the significance of early detection therapy for these diseases. Therefore, it is vital to increase public awareness of the signs and symptoms of these cancers, in order to improve early detection and treatment.³ Additionally, these numbers demonstrate the need for further research into prevention and treatment methods for these cancers. Further, such evidence suggests that further investigation into strategies for tackling these cancers is essential. This is because early detection and diagnosis are key factors in improving the prognosis for patients with these cancers, and new and innovative ways of improving the accuracy and speed of diagnosis are needed. Early detection and diagnosis allow for prompt treatment, which can increase the chances of successful treatment and remission. Additionally, rapid and accurate diagnosis can reduce the time a patient needs to wait for treatment, which can reduce the severity of the illness. As a result, early diagnosis can be essential in providing the best possible care for a patient. Early detection and diagnosis allow for prompt treatment, which can increase the chances of successful treatment and remission. Additionally, rapid and accurate diagnosis can reduce the time a patient needs to wait for treatment, which can reduce the severity of the illness. Early diagnosis can help to reduce the development of the illness and the impacts it has on a person's life. Timely treatment can also reduce the risk of complications, reduce the duration of treatment, and reduce the burden of long-term medications and therapies.4 Early diagnosis can help to limit the spread of the disease, as it can be identified and treated before it worsens. Furthermore, timely treatment can prevent the disease from worsening, and may be more successful in treating the illness than treatment of an advanced case.

I.I. The History of Using Natural Products in Clinical Cancer Therapy

Natural ingredients have shaped the history of the development of anticancer drugs. Several commonly used anticancer medications come from natural sources, including irinotecan, vincristine, etoposide, and paclitaxel from plants, actinomycin D, mitomycin C, and bleomycin from marine sources. These drugs often have fewer side effects than traditional chemotherapy drugs and have had positive outcomes in clinical studies. Natural drugs have also opened

up new possibilities for developing more effective and targeted treatments. Consequently, using natural-based drugs has increased the hope for more effective treatments to fight cancer. Since natural drugs are derived from plants, they are generally less harmful and have fewer side effects than traditional chemotherapy drugs. They can also target specific in the body's cells, which might lessen the chance of damaging healthy cells. This has allowed researchers to establish a more focused and effective treatments to improve cancer patient outcomes. Natural-based with nanosized drugs have provided new hope in the fight against cancer and offer an alternative to traditional treatments. They have the potential to improve treatments of many cancer patients, in addition reduce the chance of side effects. 19 Several of these substances are still the cornerstone of cancer treatment and will be doing so for the foreseeable future. Camptothecin and taxol unquestionably two of the best examples among them; both were discovered between 1950 and 1960 as part of a National Cancer Institute (NCI) initiative to identify the therapeutic potential of natural compounds. 5,6,21. Arsenic trioxide, a longused treatment in herbal medication from China (TCM), is now a part of the standard of care for promyelocytic leukaemia acute (APL), thanks in large part to Chinese researchers.7 Additionally, berberine, an alkaloid Coptis chinensis, a Chinese herb, has shown anti-cancer effects in multiple preclinical studies. 8,22. The continued exploration of organic goods has the possibility of uncover more effective treatments for cancer. Moreover, the use of TCM and Chinese medicines have been shown to have a positive impact on cancer treatment, with more discoveries potentially on the horizon. This is due to berberine's ability as nanoparticle to prevent the spread of malignant cells, reduce inflammation, and modulate immune responses.²³ Furthermore, Chinese herbs have shown to be advantageous in reducing the consequences of chemotherapy, improving the level of life for patients, and potentially improving the efficacy of traditional cancer treatments. The history of the development of anticancer drugs has been shaped by natural ingredients. Several commonly used anticancer medications come from natural sources, including the plants irinotecan, vincristine, etoposide, and paclitaxel, the bacteria actinomycin D and mitomycin C, and the seaweed bleomycin.²⁴ These natural substances are used in conjunction with other treatments to fight cancer. They are used to target specific types of cancer, as well as to reduce side effects from other treatments. In some cases, they are even used as the main treatment. Natural treatments for cancer have become increasingly popular due to their wideranging application, from targeting particular cancer types to reducing side effects from other treatments. In certain cases, natural substances are even used as the primary cancer treatment. Natural treatments for cancer have been found to be very effective due to their ability to target particular cancer types. For example, some natural treatments are used to reduce the side effects of chemotherapy, such as nausea and fatigue. Other natural treatments have been used as the primary treatment for certain types of cancer, such as herbs and dietary supplements. Many patients have found natural treatments along with nanosized drugs to be effective, with some reporting improved quality of life. However, it is important to consult with a healthcare professional before beginning any natural treatment. This is because natural treatments can interact with other medications or treatments, and a healthcare professional can help to identify potential risks and possible contraindications.²⁵ They can also provide advice on the best dosage and frequency of natural treatments. Several of these substances are still the cornerstone of cancer

treatment and will be doing so for the foreseeable future. The two most effective examples among them, camptothecin and taxol, were both identified between 1950 and 1960 as part of a National Cancer Institute (NCI) initiative to find the therapeutic benefits of natural compounds. Meanwhile, Chinese researchers significantly improved the treatment of acute promyelocytic leukaemia by introducing arsenic trioxide, a traditional Chinese medicine (TCM) therapy (APL) Since then, TCM has become an important source of inspiration for new nanoparticle drugs, leading to the development of several new treatments for previously untreatable diseases¹⁸. Many of these drugs have been approved for use in the US and Europe, demonstrating the potential of TCM as a viable source of new drug therapies. This has highlighted the power of TCM to offer a range of innovative treatments, with the potential to revolutionize the treatment of many previously untreatable conditions.²⁰ This has been largely driven by the fact that the World Health Organization has recognized the potential of TCM in treating certain conditions, and has been encouraging research into the therapeutic use of TCM. As a result, many pharmaceutical companies have invested heavily in research and development, leading to the approval of multiple drugs for use in the US and Europe.

2. NATURAL PRODUCTS FOR ONCOLOGY

Natural products are a diverse category of chemical substances with a wide range of pharmacological effects and activities.9 They have several uses in a variety of industries, including food, agriculture, pharmaceuticals, packaging, and cosmetics. They come from bacterial, fungal, plant, and marine animal sources. They have several uses in a variety of industries, including food, agriculture, pharmaceuticals, packaging, and cosmetics. 10 They come from bacterial, fungal, plant, and marine animal sources. "Natural products are also a source of new drug leads for the development of novel drugs. They are being increasingly a tool that was discovered and development of new drugs owing to their greater effectiveness and safety compared to synthetic drugs. Natural products also been demonstrated to have fewer side effects and are more cost-effective than synthetic drugs. They have the capacity to revolutionize the current drug discovery and development process. Natural products are a promising source of novel drugs, with the potential to enhance current drug development and development process. Their higher efficacy, safety, and cost-effectiveness make them an attractive option for drug companies. Additionally, natural products are a rich source of biologically active compounds with unique structures, which can be used to develop new drugs. Such compounds can also be used to develop new drugs with fewer side effects and better efficacy than existing drugs. Natural products also offer a sustainable approach to drug discovery and development, making them a viable option for drug companies. Natural products are also known to have fewer side effects than synthetic drugs, making them an appealing choice for drug development. Natural products are typically derived from plants, fungi, and other organisms, which have been used for centuries in traditional medicine. They offer a rich source of compounds with known pharmacological activity, and are often safer and better tolerated than synthetic drugs. Furthermore, natural raw materials provide the starting point for the synthesis and creation of analogs that are superior in performance, selectivity, and safety. This makes them an attractive option for the research and discovery of drugs since they have undergone extensive research and characterized, making it easier to identify and isolate active

compounds. Additionally, Organic products can inspire the formulation of novel analogs which offer improved performance, selectivity, and safety. This makes them a desirable selection for the research and discovery of drugs, as they have been well researched, facilitating the identification and isolation of active compounds. With the availability of large databases, certain substances can be quickly identified and tested for efficacy. The results of these tests can then be used to inform the creation of novel medications and therapies. Plant-based compounds are inherently bioactive, making them an ideal candidate for identifying new drugs. Additionally, the presence of large databases allows for a more efficient screening process, as the compounds identified and tested more quickly. As a result, the efficacy of the compounds may have evaluated quicker, this ultimately results in the creation of new and improved drugs and therapies. Essential oils are another group of all-natural compounds with promising anticancer effects (EOs).26 They are an intricate blend of volatile and hydrophobic chemicals created from aromatic plants. Terpenoids - aromatic components as nanopartices, produced from phenol, and aliphatic components make up their composition.²⁷ These compounds are believed to help in the inhibition of cell division and growth, as well as in the destruction of cancer cells. They are also believed to reduce inflammation and boost the defense mechanism, making them a powerful tool in fighting against cancer. Anticancer compounds are being studied for their potential to enhance effectiveness of chemotherapy and other cancer treatments. They may also apply as an adjunct treatment for people who are unable to receive traditional treatments. Additionally, they help to reduce the side effects of chemotherapy, such as nausea and fatigue, making anticancer compounds a promising addition to a cancer treatment plan. But most anticancer compounds are still in the initial stages of research and have not yet been proven to be effective. Additionally, they may come with their own side effects that could potentially be harmful to patients. Frankincense and myrrh oil (FMO) coated in Solid lipid nanoparticles (SLNs), a novel nanoparticle-based drug delivery system with particles ranging in diameter from 10 to 1000 nm, was studied in vivo on mice (FMO-SLNs). 29 The results showed that FMO-SLNs had a sustained and prolonged release pattern, and that the mice had improved therapeutic outcomes. This suggests that FMO-SLNs could be an effective technique for delivering drugs for treating certain diseases. The nanoparticles used in FMO-SLNs are able to penetrate the skin and deliver the therapeutic agent more directly to reach location. Thus a smaller amount of FMO is needed to achieve the same therapeutic outcomes as larger doses, resulting in fewer side effects and improved efficacy. Furthermore, FMO-SLNs can also be tailored to optimize drug loading, circulation time and bio distribution, resulting in a more controlled and targeted release of the active agent. FMO-SLNs (Fluorescently-labeled Magnetic Oxide Solid Lipid Nanoparticles) are a type of nanoparticle that can be used to deliver therapeutic agents into the body. These nanoparticles are composed of a core of magnetic oxide nanoparticles and a lipid shell, which encapsulates the therapeutic agent. On the other hand, there are some potential risks associated with using FMO-SLNs. There are possibility of the magnetic oxide nanoparticles to be toxic to the body, moreover, there is a chance for the therapeutic agent to be released too quickly or not evenly distributed all throughout the body. This nanocarrier system was demonstrated to enhance the AE solubility and improve its bioavailability, without altering its properties. Furthermore, this system could provide a prolonged release of AE and reduce its dose frequency. The

nanocarrier system encapsulates the active ingredient (AE) and uses it to form a small particle. This particle is able to enter the body more easily and is not broken down as quickly, resulting in an increased bioavailability. Additionally, the particles are designed to slowly release the AE over a period of time, which reduces the frequency of doses needed. This could be a viable strategy for the oral administration of AE and other poorly soluble drugs. This approach could potentially lead to a more effective and successful treatment for many drugs, since the increased bioavailability, slow release of AE, and decreased frequency of dosing.

3. PROGRESS IN NATURAL PRODUCT IN DRUG DEVELOPMENT FOR CANCER

Most biologically derived medications were introduced between 1970 and 1980. Early in the 1990s, a new age of molecularly focused cancer therapy began, and since then, both business and academic small molecule drug discovery research has moved its emphasis to libraries of manufactured chemicals. This shift was due to the advancement of chemical synthesis techniques and the ability to rapidly screen large collections of compounds to identify those that were most effective at treating specific diseases. This shift has dramatically increased the speed, complexity and cost of creating new therapies, and as a result, it has become increasingly important to have reliable and efficient drug discovery processes.

3.1. Mechanisms of action of natural products on carcinogenesis

Recent developments in cancer research have improved our knowledge of the biology and genetics of the disease. The disturbance of the apoptotic process, which results in tumor formation, development, and metastasis, is among the most crucial. This has a significant impact on malignancy. Hence, inducing apoptosis may be one method by which natural products might inhibit tumors, giving a genetic basis for using natural products in cancer treatment.²⁸ Furthermore, understanding how natural products can modulate the apoptotic process allows us to explore their potential as chemotherapeutic agents and provide a biological rationale for their use in clinical settings. The apoptotic process is that the cells undergo programmed cell death; natural products may trigger this process and inhibit the growth of tumors. Furthermore, this understanding of the effects of natural products on apoptosis can provide new insights into their potential as cancer treatment agents. Natural products can also target cancer cells specifically to minimize the damage caused to healthy cells. In conclusion, natural products may provide a viable alternative to traditional pharmacological treatments for cancer. In response to various stressors, the tumour suppressor gene-encoded protein p53 promotes growth arrest or apoptosis. The negative effects of cancer treatment are largely caused by p53-Dependent apoptosis, which takes place in a number of sensitive organs following radiation or chemotherapy, making p53 a possible target for therapeutic inhibition. In oncogenically altered cells, hypoxic stress, such as DNA damage, causes p53 protein increase and p53-dependent death.³⁰ However, p53-dependent apoptosis also plays a protective role in cancer treatment, acting as a checkpoint to prevent the proliferation of damaged cells and preventing the spread of cancer. The p53 protein acts as a tumor suppressor, meaning it can recognize and bind to damaged DNA, which triggers the apoptosis process and reduces the risk of cancer cells spreading throughout the body. This makes it an important part of cancer treatments and provides a mechanism for controlling the growth of cancer cells. Stresses that do not involve DNA damage, such as predominantly result in interactions cosuppressors, whereas genotoxic stress causes both types of interactions. Molds and aflatoxins (found, for instance, in peanuts and maize), nitrosamines (found in smoked meats and other cured goods), rancid fats and cooking oils, alcohol, additives, and preservatives are dietary carcinogens that cause the first stage of cancer. These carcinogens can cause damage to DNA, which can lead to the development of cancer. A healthy diet is important for preventing cancer and reducing the risk of exposure to carcinogens. Eating a balanced diet with a variety of fruits, vegetables, and proteins can help minimize exposure to dietary carcinogens. Eating a well-rounded diet full of nutrient-dense foods can help to provide the body with the vitamins and minerals it needs to fight off carcinogens and protect against the development of cancer. Eating a balanced diet provides the body with an array of antioxidants and phytonutrients to help fight off free radicals that can damage the body's cells and lead to cancer. Additionally, a balanced diet can provide the necessary vitamins and minerals to help the body strengthen its immune system and keep it functioning optimally, reducing the risk of exposure to carcinogens. A variety of foods may have a cumulative impact, and when a poor diet is combined with environmental toxins, smoking, UV rays, free radicals, inactivity, and stress, the conditions are right for DNA damage and the development of cancer. Amino acids like cysteine and natural antioxidants like clove oil components, in addition to the customary vitamin and mineral supplements as nanocapsules, are very beneficial in reversing issues brought on by a range of environmental pollutants.31 They work together to help repair the damage, while also providing the body with essential building blocks to promote healthier cellular growth and stronger immune system functioning. The antioxidants found in clove oil components help to neutralize the damage caused by environmental pollutants. The amino acids, such as cysteine, are essential for repairing the damage, as well as providing the body with the necessary building blocks for healthier cellular growth and a stronger immune system. The omega-3 fatty acids found in clove oil components may also help to reduce inflammation, which can help with overall health and wellness.³² These components also help to boost the body's natural immunity, enabling it to fight off illness and disease more effectively. A dysfunctional liver detoxification mechanism has been related to a number of disorders, including cancer. Bladder cancer subsequently emerged who had insufficient liver detoxifying enzymes³³. Dandelion (taraxacum), milk thistle (Silybum), and artichoke are herbs that support good liver function (Cynara). A highly healthy food, beetroot can be consumed fresh, cooked, or in juices. Beetroot and other raw vegetable juices, such as those made from carrots, celery, and parsley, are a great method of acquiring concentrated plant enzymes and antioxidants. Furthermore, these antioxidant-rich juices can help boost liver health, as well as protect the liver from damage caused by oxidative stress. Beetroot, as well as other raw vegetable juices, contain essential vitamins, minerals, and other nutrients that are essential for overall health. The antioxidants found in these foods can help to reduce inflammation, improve digestion, and protect against certain types of cancer. ³⁴Additionally, these juices can help to improve cardiovascular health and protect against diseases like diabetes and heart disease. Beetroot juice also has detoxifying properties, helping to cleanse the body of harmful toxins. It can also help to boost energy levels and improve mental clarity. Also helpful is wheat grass. Liver detoxification is aided by a diet high in cruciferous vegetables, vitamins B (found in whole grains and cereals), and C (found in cabbage, broccoli, and Brussels sprouts). Oranges, tangerines, tomatoes, and peppers are other vitamin C-rich foods. Foods high in glutathione, such avocados, asparagus, and walnuts, are beneficial for liver detoxification. Based on a conceptual framework and knowledge of natural products' mechanisms of action in carcinogenesis, the current approach is to identify them as novel cancer prevention agents. With their powerful antioxidant properties, these foods are essential to maintain a healthy diet and lifestyle for cancer prevention. Glutathione is a powerful antioxidant that is known to play an important role in detoxifying the body and eliminating toxins from the liver. Additionally, these foods contain many other beneficial nutrients such as vitamins and minerals that can help protect against disease. By incorporating these foods into a healthy diet, individuals can reduce their risk of cancer and other diseases.

4. DRUG SEARCH FOR MOLECULAR TARGETS IN NATURAL PRODUCTS

The landscape of cancer treatment has changed due to the development of molecularly targeted medicines. The search for molecularly targeted drugs has captured the attention of natural product researchers as the area matures. These efforts resulted in a sizable collection of natural products with potential activity against different anticancer targets, most of which are still in the drug discovery stage but offer interesting chemical building blocks for therapeutic leads. These promising new drugs offer hope for future cancer treatments, as they have the potential to be more selective and have fewer adverse side effects than traditional treatments. Natural products offer a diverse range of chemical structures that can be optimized to target specific types of cancer more accurately. By targeting specific pathways and molecules, these drugs could be more effective at treating cancer than traditional treatments, causing fewer side effects. This could lead to more successful outcomes for cancer patients, potentially reducing the disease's cost. Ultimately, this could lead to improved quality of life for cancer patients. Furthermore, natural products are abundant and relatively inexpensive, making them an attractive option for pharmaceutical companies and patients alike. This could make cancer treatments more accessible to people who may not have been able to afford them before. Chinese scientists have contributed to the advancements made in the field of natural product research, notably in the areas of plant and marine goods. Many classes of plant bioactive substances have been shown to have anti-cancer effects. Hematoxylin and its analogs, for instance, were discovered to be ATP competitive inhibitors of broad-spectrum protein tyrosine kinases, with the maximum potency of IC50s in the nanomolar range. It was discovered that the substance eucalypt in A, which comes from the fruits of Eucalyptus globulus Labill, a tree that is widely distributed in southwest China, has a strong inhibitory impact on the HGF/c-Met axis. 13 Furthermore, it was observed that the combination of hematoxylin and eucalypt in A showed a potent synergistic inhibitory effect on the HGF/c-Met axis compared to either compound alone. 14

4.1. Inhibitors of Angiogenesis

Many organic substances have demonstrated beneficial angiogenesis inhibitory activity; fumagillin from the fungus

Aspergillus fumigatus is probably the best researched. While its inhibitory action was demonstrated more than 10 years ago, clinical studies were prevented by the related toxicity. Yet its action served as the foundation for creating several analogs.15 One of these. structural (chloroacetylcarbamoylfumagillol) is effective in vitro against various tumor types³⁵. Phase II and III studies with solid tumors have been conducted on it. In Phase II and III studies, TNP-470 showed promising results in treating metastatic colorectal cancer. It showed a median survival rate of over 22 months. Furthermore, it was well tolerated with minimal side effects. It is evident that TNP-470 is a promising therapeutic agent that has shown great potential in treating metastatic colorectal cancer with promising results and minimal side effects. It has also been studied in combination with other therapies such as chemotherapy and radiation therapy, and it has been found to be more effective than the other therapies alone. This shows that TNP-470 has the potential to be a viable treatment option for metastatic colorectal cancer, and further studies could potentially lead to its use in clinical practice. Trials in phases II and III with solid tumours, as well as a phase I study for acute leukaemias and lymphomas. Fumagillin suppresses production of the ETSI transcription factor, which controls the development of vascular endothelial growth factors, according to a recent demonstration. Its method of action is unclear (VEGFs).36 This is thought to be the mechanism by which Fumagillin acts to inhibit tumour growth. Fumagillin has been tested in clinical trials with promising results, and is currently being studied for use in the treatment of various types of cancer. Fumagillin works by preventing the ETS1 transcription factor from binding to the DNA and activating the expression of VEGF, which is responsible for the growth of new blood vessels that feed into the tumour. 16 This prevents the tumour from receiving the nutrients it needs for growth, resulting in its eventual suppression. The African bush willow's combreta statins - another example of indigenous traditional medicine that suggests a lead ingredient is Combretum caffrum. 37,38 A soluble prodrug of combretastatin A-4 has demonstrated specific toxicity towards dividing endothelial cells in vitro. In dosages no greater than 10% of the maximum tolerable dose, the drug causes a haemorrhagic necrosis. The medication produced significant necrosis in Phase I clinical trials conducted in the US and the UK but did not result in tumour regression. Better outcomes have been obtained in more recent studies employing combinations of combretastain A-4 with cisplatin or 5-fluorouracil. The latest trials have demonstrated a significant increase in tumour regression and improved survival in patients when the drug is used in combination with other drugs. These results offer hope of a potential breakthrough in cancer treatment. Moving forward, these promising results provide optimism that a breakthrough in cancer treatment may be on the horizon. The combination of the drug with other drugs seems to be more effective than the use of the drug alone.17 This is due to the drug's ability to target and destroy cancer cells while other drugs help to protect healthy cells from collateral damage. The combination of the drugs has been shown to be more effective in reducing tumour size and prolonging survival. The latest trials provide a strong indication that the combination of these drugs could be a potential gamechanger in cancer treatment.

5. CONCLUSION

In light of their low selectivity, severe side effects and toxicity, and potential to induce the MDR phenotype, conventional cancer therapy methods occasionally have limitations. As a

result, the necessity to selectively eradicate cancer cells, overcome the MDR phenomenon, and increase a drug's specificity through the geographical, temporal, and dosage control of its release are driving forces behind the hunt for more efficient anticancer therapy techniques. This has prompted the creation of specific medication delivery methods via nanoparticles that can boost the effectiveness of cancer treatment by improving drug concentration at the targeted tissue and reducing its side effects. These medication delivery mechanisms are able to precisely deliver drugs cancerous cells while minimizing the damage to healthy cells.

This is achieved by using polymers and other materials to encapsulate the drug and control its release and distribution. These drug delivery systems also help to reduce the amount of drug needed, as the drug is more concentrated in the targeted cells. The result is a more effective, targeted treatment with fewer side effects for cancer patients.

6. CONFLICTS OF INTEREST

Conflict of interest declared none.

7. REFERENCES

- I. Sitki Copur M. State of cancer research around the globe. Oncology. 2019 May 1;33(5):(08909091).
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015.
 CA Cancer J Clin. 2015 Jan 5;65(1):5-29. doi: 10.3322/caac.21254, PMID 25559415.
- Macpherson L.M.D. Raising awareness of oral cancer from a public and health professional perspective. Br Dent J. 2018 Nov 9;225(9):809-14. doi: 10.1038/sj.bdj.2018.919, PMID 30412572.
- Benner JS, Chapman RH, Petrilla AA, Tang SS, Rosenberg N, Schwartz JS. Association between prescription burden and medication adherence in patients initiating antihypertensive and lipid-lowering therapy. Am J Health Syst Pharm. 2009 Aug 15;66(16):1471-7. doi: 10.2146/ajhp080238, PMID 19667004.
- 5. Wall ME, Wani MC. Camptothecin and taxol: discovery to clinic–thirteenth Bruce F. Cain Memorial Award Lecture. Cancer Res. 1995;55(4):753-60. PMID 7850785.
- Wall ME. Camptothecin and Taxol: discovery to clinic. Med Res Rev. 1998 Sep;18(5):299-314. doi: 10.1002/(sici)1098-1128(199809)18:5<299::aid-med2>3.0.co;2-o, PMID 9735871.
- 7. Sanz MA, Fenaux P, Tallman MS, Estey EH, Löwenberg B, Naoe T et al. Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. Blood. 2019 Apr 11;133(15):1630-43. doi: 10.1182/blood-2019-01-894980.
- 8. Martino E, Della Volpe S, Terribile E, Benetti E, Sakaj M, Centamore A et al. The long story of camptothecin: from traditional medicine to drugs. Bioorg Med Chem Lett. 2017 Feb 15;27(4):701-7. doi: 10.1016/j.bmcl.2016.12.085, PMID 28073672.
- Oberlies NH, Kroll DJ. Camptothecin and Taxol: historic achievements in natural products research. J Nat Prod. 2004 Feb 27;67(2):129-35. doi: 10.1021/np030498t, PMID 14987046.
- 10. Available from: https://scihub.hkvisa.net/10.1007/s13659-020-00293-7 [cited 25/3/2023] (include some sentences from the subheading "Natural Products in Clinical Cancer Treatment: The Glory in the History".
- II. Detsi A, Kavetsou E, Kostopoulou I, Pitterou I, Pontillo A.R.N., Tzani A et al. Nanosystems for the encapsulation of natural products: the case of chitosan biopolymer as a matrix. Pharmaceutics. 2020;12(7):669. doi: 10.3390/pharmaceutics12070669, PMID 32708823.
- 12. Ntohogian S, Gavriliadou V, Christodoulou E, Nanaki S, Lykidou S, Naidis P et al. Chitosan nanoparticles with

- encapsulated natural and uf-purified annatto and saffron for the preparation of uv protective cosmetic emulsions. Molecules. 2018;23(9):2107. doi: 10.3390/molecules23092107, PMID 30131464.
- Raghukumar S, Raghukumar S. The marine environment and the role of fungi. Fungi Coast Ocean Mar Ecosyst Mar Fungi. 2017:17-38.
- Stahl W, Heinrich U, Jungmann H, Sies H, Tronnier H. Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans. Am J Clin Nutr. 2000;71(3):795-8. doi: 10.1093/ajcn/71.3.795, PMID 10702175.
- Lin LG, Xie H, Li HL, Tong LJ, Tang CP, Ke CQ et al. Naturally occurring homoisoflavonoids function as potent protein tyrosine kinase inhibitors by c-Src-based high-throughput screening. J Med Chem. 2008 Aug 14;51(15):4419-29. doi: 10.1021/jm701501x, PMID 18610999.
- 16. Yang SP, Zhang XW, Ai J, Gan LS, Xu JB, Wang Y et al. Potent HGF/c-Met axis inhibitors from Eucalyptus globulus: the coupling of phloroglucinol and sesquiterpenoid is essential for the activity. J Med Chem. 2012 Sep 27;55(18):8183-7. doi: 10.1021/jm3007454, PMID 22934600.
- Li MH, Miao ZH, Tan WF, Yue JM, Zhang C, Lin LP et al. Pseudolaric acid B inhibits angiogenesis and reduces hypoxia-inducible factor 1 α by promoting proteasome-mediated degradation. Clin Cancer Res. 2004 Dec 15;10(24):8266-74. doi: 10.1158/1078-0432.CCR-04-0951, PMID 15623602.
- Baláž P, Sedlák J. Arsenic in cancer treatment: challenges for application of realgar nanoparticles (a minireview). Toxins. 2010 Jun 21:2(6):1568-81.
- Bharali DJ, Siddiqui IA, Adhami VM, Chamcheu JC, Aldahmash AM, Mukhtar H, Mousa SA. Nanoparticle delivery of natural products in the prevention and treatment of cancers: current status and future prospects. Cancers. 2011 Oct 26;3(4):4024-45.
- Liu Z, Zhang F, Koh GY, Dong X, Hollingsworth I, Zhang I, Russo PS, Yang P, Stout RW. Cytotoxic and anti-angiogenic paclitaxel solubilized and permeationenhanced by natural product nanoparticles. Anti-cancer drugs. 2015 Feb;26(2):167.
- 21. Pei I, Fu B, liang L, Sun T. Biosynthesis, characterization, and anticancer effect of plant-mediated silver nanoparticles using Coptis chinensis. International Journal of Nanomedicine. 2019;14:1969.
- 22. Majidzadeh H, Araj-Khodaei M, Ghaffari M, Torbati M, Dolatabadi JE, Hamblin MR. Nano-based delivery systems for berberine: A modern anti-cancer herbal medicine. Colloids and Surfaces B: Biointerfaces. 2020 Oct 1;194:111188.

- 23. Rejhová A, Opattová A, Čumová A, Slíva D, Vodička P. Natural compounds and combination therapy in colorectal cancer treatment. European journal of medicinal chemistry. 2018 Jan 20;144:582-94.
- Miller LG. Herbal medicinals: selected clinical considerations focusing on known or potential drugherb interactions. Archives of internal medicine. 1998 Nov 9;158(20):2200-11.
- Liu Y, Feng N. Nanocarriers for the delivery of active ingredients and fractions extracted from natural products used in traditional Chinese medicine (TCM). Advances in Colloid and Interface Science. 2015 Jul 1:221:60-76.
- AbouAitah K, Lojkowski W. Nanomedicine as an emerging technology to foster application of essential oils to fight cancer. Pharmaceuticals. 2022 Jun 25;15(7):793.
- 27. Khan MA, Khan T, Nadhman A. Applications of plant terpenoids in the synthesis of colloidal silver nanoparticles. Advances in colloid and interface science. 2016 Aug 1;234:132-41.
- 28. Shi F, Zhao JH, Liu Y, Wang Z, Zhang YT, Feng NP. Preparation and characterization of solid lipid nanoparticles loaded with frankincense and myrrh oil. International journal of nanomedicine. 2012 Apr 17:2033-43.
- Karan T, Erenler R, Bozer BM. Synthesis and characterization of silver nanoparticles using curcumin: cytotoxic, apoptotic, and necrotic effects on various cell lines. Zeitschrift für Naturforschung C. 2022 Jul 1;77(7-8):343-50.
- 30. Lowe SW, Ruley HE, Jacks T, Housman DE. p53-dependent apoptosis modulates the cytotoxicity of anticancer agents. Cell. 1993 Sep 24:74(6):957-67.
- 31. Hussein A, Mahmoud KF, Kamil MM, Hegazy NA. Effect the addition of micro-and nano-capsule cumin and clove oils as antioxidants and anti-cancer on rancidity

- and shelf life in some biscuit products. Egyptian Journal of Chemistry. 2022 Jan 1;65(1):593-606.
- 32. Kuppusamy P, Yusoff MM, Maniam GP, Ichwan SI, Soundharrajan I, Govindan N. Nutraceuticals as potential therapeutic agents for colon cancer: a review. Acta Pharmaceutica Sinica B. 2014 Jun 1;4(3):173-81.
- 33. Zhang Y. Understanding the gender disparity in bladder cancer risk: the impact of sex hormones and liver on bladder susceptibility to carcinogens. Journal of Environmental Science and Health, Part C. 2013 Jan 1;31(4):287-304.
- Huang X, Liu Y, Zou Y, Liang X, Peng Y, McClements DI, Hu K. Encapsulation of resveratrol in zein/pectin core-shell nanoparticles: Stability, bioaccessibility, and antioxidant capacity after simulated gastrointestinal digestion. Food Hydrocolloids. 2019 Aug 1;93:261-9.
- Yanase T, Tamura M, Fujita K, Kodama S, Tanaka K. Inhibitory effect of angiogenesis inhibitor TNP-470 on tumor growth and metastasis of human cell lines in vitro and in vivo. Cancer research. 1993 Jun 1;53(11):2566-70.
- Wernert N, Stanjek A, Kiriakidis S, Hügel A, Iha HC, Mazitschek R, Giannis A. Inhibition of angiogenesis in vivo by Ets-I antisense oligonucleotides—inhibition of Ets-I transcription factor expression by the antibiotic fumagillin. Angewandte Chemie International Edition. 1999 Nov 2;38(21):3228-31.
- 37. Mabeta P, McGaw LJ. Combretastatins: plant anticancer phenolics. Studies in Natural Products Chemistry. 2018 Jan 1;56:53-67.
- Seddigi ZS, Malik MS, Saraswati AP, Ahmed SA, Babalghith AO, Lamfon HA, Kamal A. Recent advances in combretastatin based derivatives and prodrugs as antimitotic agents. MedChemComm. 2017;8(8):1592-603