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BIOSYNTHESIS OF NANOPARTICLES FROM PLANT EXTRACTS AND THEIR APPLICATIONS IN MEDICAL TREATMENTS AND DRUG DELIVERY: A REVIEW ARTICLE

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Abstract

Nanotechnology is one of the modern technologies used in many fields, including agriculture, industry, and medicine. Nanoparticles are synthesized in many ways, with the biological method using microorganisms or plant extracts is among the easy, quick, cheap, and environmentally safe ways of doing. Green nanotechnology is an exciting and emerging field of technology and generation that combines the concepts of green chemistry with the advantages of sustainability and overall protection of the environmen. Green chemistry methods are suitable for producing and processing hazardous chemicals that threaten human health and the environment. This technology requires extensive experience in dealing with the raw materials, especially in the elements and metals used to transform them into nanomaterials and the resulting side effects and chemical reactions. nanotechnology has achieved a systemic breakthrough and metal nanoparticles (green nanoparticles) have received much attention due to their physiological, technological and chemical differences. Biological technology is of great importance because it produces green nanoparticles in an environmentally friendly, simple, easy, fast and cost-effective way. Phenolic amino acids, flavonoids, terpenoids, and proteins are examples of reducing and oxidizing agents. This article reviews the latest studies on the biosynthesis of metal nanoparticles using plant extracts. Researchers use extracts of various plant parts (roots, stems, leaves, fruits, fruit peels, seeds) to produce nanoparticles of many metals, the most important being silver, gold, and oxides of some metals such as iron oxide and other metal oxides. This review also discusses some examples of the use of metallic nanomaterials in treating bacterial infections, viruses, and cancerous diseases, and their widespread use in drug delivery.

Keywords: Biosynthesis, Nanoparticles, Plant extracts, Anticancer.

التخليق الحيوي للجسيمات النانوية من المستخلصات النباتية وتطبيقاتها في المعالجات الطبية والتوصيل الدوائي: مراجعة مقال

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الخلاصة

تعد تقنية النانو من التقنيات الحديثة التي تدخل في مجالات عديدة منها الزراعة والصناعة والطب. يتم تخليق الجسيمات النانوية بطرائق عديدة، وتعد الطريقة الحيوية من الطرائق السهلة، السريعة، الرخيصة والآمنة بيئياً، والتي تتم باستخدام الكائنات الحية الدقيقة أو المستخلصات النباتية. تكنالوجيا النانو الخضراء مجالًا مثيرًا وصاعدا للتكنولوجيا والجيل الذي يجمع بين مفاهيم الكيمياء الخضراء ومزايا القدرة على الاستدامة والحماية العامة من الجنس البشري. تعد طرق الكيمياء الخضراء طرق مناسبة لإنتاج ومعالجة المواد الكيميائية الخطرة التي تهدد صحة الإنسان والبيئة. وتتطلب هذه التقنية خبرة مكثفة في التعامل مع المواد الخام، لا سيما في المواد والمعادن المستخدمة لتحويلها إلى مواد نانوية وما ينتج عنها من اثار جانبية وتفاعلات كيميائية. في القرن الحادي والعشرين، أصبحت تكنولوجيا النانو طفرة منهجية. لاقت الجسيمات النانوية المعدنية (الجسيمات النانوية المصنوعة بطريقة خضراء) الكثير من الاهتمام بسبب اختلافها الفسيولوجي والتكنولوجي والكيميائي. وتحظى التقنية البيولوجية بأهمية كبيرة لأنها تنتج جسيمات نانوية خضراء بطريقة صديقة للبيئة وبسيطة وسهلة وسريعة وفعالة من حيث التكلفة. تعتبر الأحماض الأمينية الفينولية والفلافونويدات والتيربينويدات والبروتينات أمثلة على العوامل المختزلة والمؤكسدة. تشير هذه الدراسة المرجعية أحدث الدراسات حول التصنيع الحيوي للجسيمات

النانوية المعدنية باستخدام المستخلصات النباتية. استخدم الباحثون مستخلصات اجزاء النبات المختلفة (جذور، سويق، اوراق، ثمار، قشور ثمار، بذور) لإنتاج الجسيمات النانوية للعديد من المعادن أهمها الفضة، الذهب واكاسيد بعض المعادن مثل اوكسيد الحديد وغيرها من الاكاسيد المعدنية. كما تتناول الدراسة بعض الامثلة حول استخدام المواد النانوية المعدنية في معالجة الاصابات البكتيرية والفايروسات والامراض السرطانية، واستخدامها بشكل واسع في التوصيل الدوائي.

كلمات مفتاحية: التصنيع الحيوي، الجسيمات النانوية، المستخلصات النباتية، المضادات السرطانية.

Introduction

The word "nano" is derived from the Greek word "nanos", meaning "dwarf". A nanometer is one billionth of a meter, equivalent to 10^{-9} m. To put this in context, a single nanometer measures three carbon atoms lined up next to each other, the cold virus is about 100 nm, and the average diameter of a human hair is about 100,000 nm (46), (Figure 1, A). A nanomaterial is within the nanoscale if one of its dimensions does not exceed 100 nm.

The science that deals with the applications of using these materials is called nanotechnology (64), (Figure 1, C). Nanotechnology is one of the most important technologies in many fields, as it depends on the synthesis of nanoparticles (NPs). Metals differ from their constituent nanoparticles in terms of their properties depending on the geometry of their metal particles (59), Of late, interest in the formation of nanoparticles using nanotechnology has increased especially in the medical, biological, agricultural, environmental, and industrial fields (41, 59 and 101).

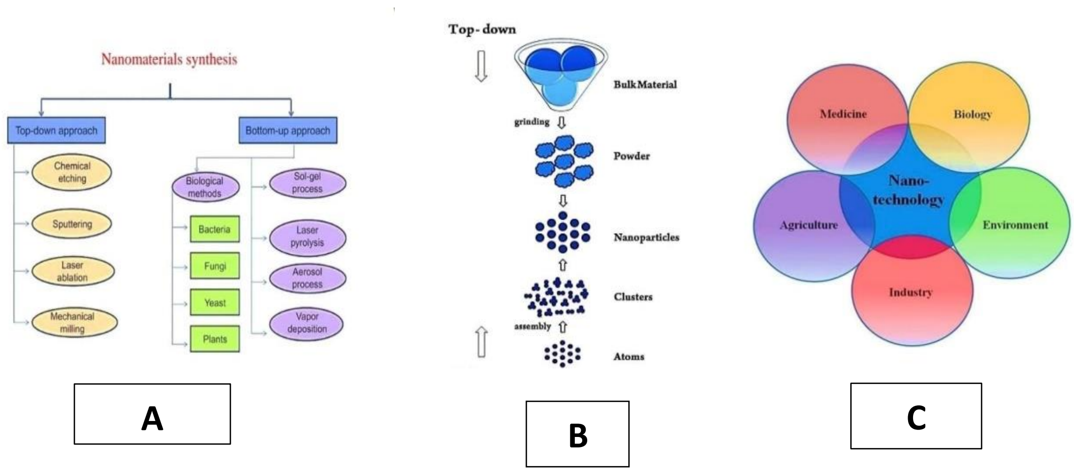

Figure 1: A: different types of processes for synthesizing nanomaterials, B: main methods used in synthesizing nanomaterials, C: the multidisciplinary field of nanotechnology.

The Science Citation Index Expanded during 2001-2010 to shows steady growth in the area of nanotechnology as well as published research on the subject (21), as shown in (Figure 2).

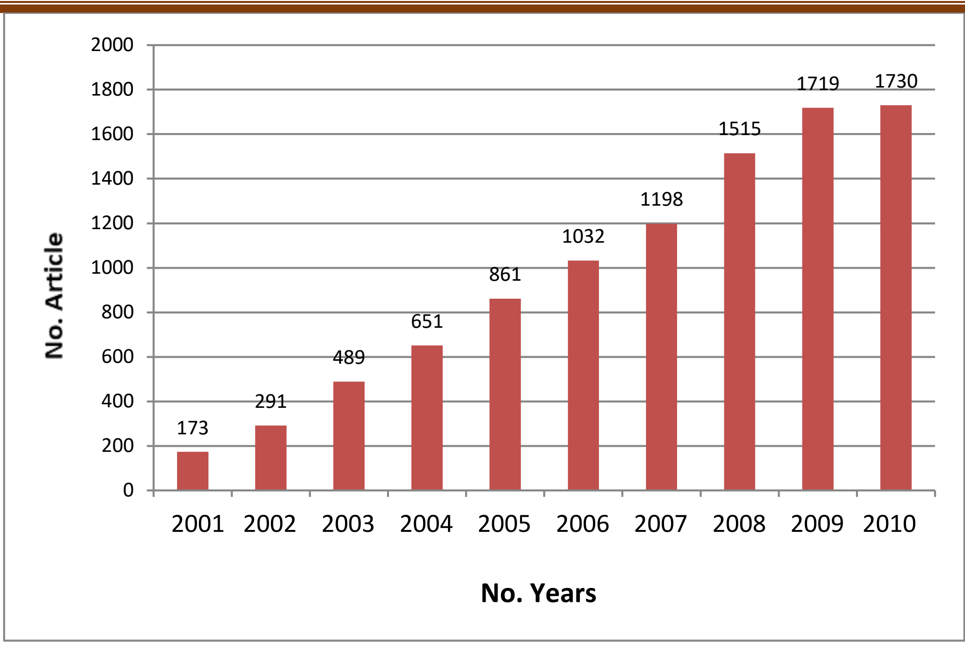

Figure 2: Number of Article published in the nanotechnology field (102).

The importance of nanomaterials derives primarily form their high surface area. Due to their extremely small size, this feature increases its contact surface with other objects (36 and 111). Particles are synthesized as nanoparticles in one of two ways, i.e., building from the bottom up and, through engineering Building nanomaterials begin from their ions through, chemical methods and vitality, or destruction from top to bottom, through physical methods such as grinding, for example (97 and 112), (Figure 1, B).

Biosynthesis of nanoparticles on the other hand is done using metabolites of microorganisms such as (viruses, bacteria, actinomycetes, true fungi including yeasts, and algae or plant extracts. According to various studies (2, 47 and 88). This method is environmentally friendly, does not require energy, and is cheap and fast.

Contains a scientific database of more than 159 articles on biosynthesis for nanoparticles, which meet the research criteria. It began in a year 2003, and scientific production in this field continued slowly until 2009. in 2010, the number of published scientific papers increased three times, and the largest number was recorded in 2015 - 2016, peaking in 2016, with 39 papers of scientific.

This paper discusses the latest research on the biosynthesis of the most important nano-mineral materials using plant extracts and applications of nanotechnology in medical fields.

Biosynthesis of nanoparticles using plant extracts:

Plants contain organic compounds such as flavonoids, amino acids and carboxylates, ketones, phenols and proteins which are examples of reduced and oxidizing agents (Figure 3). These materials play an important role in (self-assembly) (1) and in producing nanoparticles in an easy, fast, and environmentally safe manner.

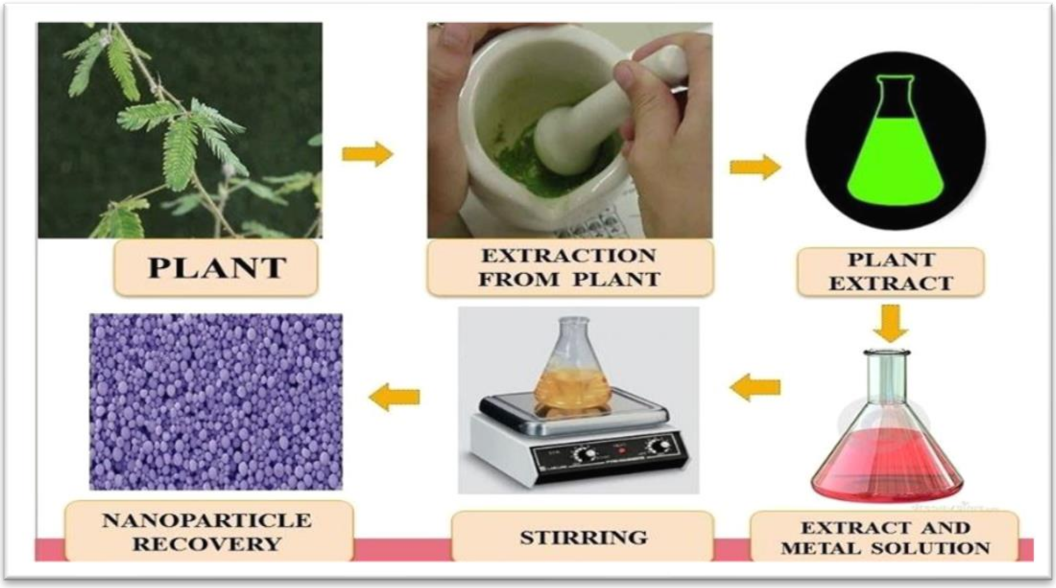

Figure 3: Extraction of nanomaterials from different plants.

Biosynthesis of silver nanoparticles:

Researchers have given silver nanoparticles special attention because of their properties such as high thermal and electrical conductivity, chemical stability, high catalytic activity, and antimicrobial activities (53 and 115), and they are used nano in several industrial fields, including wound dressings clothing, cosmetics, sports shoes, etc. Table1 shows some important research on the biosynthesis of silver nanoparticles using plant extracts from 2019-2020.

The aqueous extract of the ginger root (Zingiber officinale L.) was used to manufacture silver nanoparticles by heating the mixture of plant extract with silver nitrate ($AgNO_3$) at a high temperature 60 °C (20 and 95), to obtain silver nanoparticles (20.4 nm) after about three hours. Others (23 and 99) have used aqueous extract of beetroot (Beta vulgaris L.), where the roots were washed under a water tap and later in sterile distilled water, sliced into small pieces, and ground. The suspension was then run through a filter with a pore diameter of 22 micrometers, and 10 ml of root extract was added to 90 ml of silver nitrate solution (1 mol/L) and the mixture was mixed well. After 25 minutes, the color of the mixture was observed to change to dark brown, indicating the formation of silver nanoparticles. Images from the transmission electron microscope showed the particles to be spherical in shape with an, average diameter of 52.4±3.6 nm. These particles have proven their effectiveness in the laboratory against cancer cells. The plant stem was used in the biosynthesis of silver nanoparticles using. jasmine stem (Jasminum auriculatum Vahl) at room temperature. These particles were spherical in shape with dimensions of 10-20 nanometers after two hours of reaction, and had antibacterial activity (19 and 109). In another study, Nigeria Cowpea stalk (Vigna unguiculata L.) was used in the biosynthesis of silver nanoparticles. The legs were washed with water tap and then with distilled water and left to air dry. Then 40 g was placed in 400 ml of distilled water and boiled for 45 minutes, and then allowed to cool. To manufacture silver nanoparticles, 50 ml of plant extract was added to 100 ml of silver nitrate solution and left to mix for 5 hours. This resulted in the was the formation of silver nanoparticles (28 and 108). As for plant leaves, they have been widely used in the field of biosynthesis of silver nanoparticles. Researchers have used the aqueous extract of Melia azedarach L. To produce it in 10 minutes. The resulting particles were spherical in shape ranging, between 18 and 30 nm, and found to have active antifungal properties (54, 94 and 106).

For seed extract, the aqueous extract of pomegranate seeds (Punica granatum L.) was used in an experiment conducted in Iran. The seeds were dried for 30 days in the shade, ground, and 8g of the seed powder was added to 100 ml distilled water and placed in a water bath a 60°C for 30 minutes, after filtering a silver nitrate solution was added (1 mol/L) at a ratio of 9:1 and the mixture left under sunlight for 10 minutes. It was observed that silver nanoparticles were formed in a record time of 30 seconds, with their sizes ranging from 19-54 nm (67, 87 and 91).

Table 1: Biosynthesis of silver nanoparticles using different plant parts.

Scientific name	Common name of plant	Plant's part	NPs size (nm)	Synthesizing conditions	References
Allium sativum (Lillacea)	Garlic	peel	29.17	50-60°C, 3 h.	3,71
Borassus aethiopum Mart	African fan palm	Roots	Not determined	80 ° C, 30 min	27,80
Zingiber officinale L.	Ginger	Roots	20.4	60°C, 3.5 h.	20,73
Beta vulgaris L.	Beet	Roots	52.4-3.6	Room temp., 25 min	23,81
Vigna anguiculata L.	Cowpea	Stem	25	Room temp., 5 h.	28,84
Jasminum auriculatum Vahl	Jasmin	Stem	10-20	Room temp., 2 h.	19,72
Citrus sinensis L.	Orange	Fruits peel	50-5	90 ° C, 20 min.	104,86
Melia azedarach L.	Chinaberry	Leaves	18-30	Room temp., 10 min.	54,90
Annona Muricata	Graviola	Leaves	22-28	27 ° C , 24 h.	107,82
Moringa oleifera Lam	Horseraddish	Flowers	8	Sun light, 30 min.	22,73
Aerva lanata L.	Knotgrass	Flowers	90	Sun light, 30 min.	57,66
Nauclea Latifolia Smith	African peach	Fruits	12	Sun light, 24-72 h.	74,77
Punica granatum L.	Pomegranae	Seeds	19-54	Sun light, 30sec.	67,68
Tamarindus indica L.	Tamarind	Fruits peel	20-52	45 ° C, 2 h.	39,79
Curcuma longa L.	Curcumin	Roots	30	60°C, 1 h.	8,52
Curcuma longa L.	Curcumin	Roots	30	60°C, 1 h.	98,76
Cascuta reflexa Roxb	Dodder	Flowers	20-50	Sun light, 4 h.	69,70
citrus lemon	lemon	Fruits peel	30-50	70 °C, 25 min	107,83

Biosynthesis of gold nanoparticles:

The biosynthesis of gold nanoparticles has gained much interest in, the field of biomedicine, or what is now known as nanomedicine, due to its effectiveness as an antibacterial, antifungal, anti-cancer and antioxidant agent (56 and 105). it is also used to detect tumors, diagnose breast cancer genetics, hereditary disorders, and in the fields of photography, and phototherapy (45 and 62). Some studies on the biosynthesis of gold nanoparticles using plant extracts are shown in Table 2, (55 and

114). The fern root extract (Cibotium barometz L.) was prepared by first washing the roots several times with distilled water, and drying, and grinding them to obtain a powder, following which 5g was weighted and added to 100 ml of distilled water. The contents were boiled for 30 minutes, and the extract filtered and centrifuge to remove any impurities. A $HAuCl_4.3H_2O$ solution was added to 5 ml of plant extract to obtain the final concentration of 1 mol/L, and the mixture heated at 80°C. The color of the mixture gradually began to change until it turned red in 25 minutes. The electron microscope images showed that the gold nanoparticles formed were spherical in shape and ranged from 5-20 nm. Another study use bauhinia extract or leaf (Bauhinia purpurea L.) as a catalyst to obtain the gold nanoparticles using microwave radiation. The reaction ended within 30 minutes and produced gold nanobodies of various shapes (hexagonal). Trimeric and bacillus have proven their effectiveness as antimicrobial and anti-cancer antibodies and in oxidation (58 and 113).

Table 2: Biosynthesis of gold nanoparticles using different plant parts.

Scientific name	Common name of plant	Plant's part	NPs size (nm)	Synthesizing conditions	References
Euphorbia fischeriana	Spurge	Roots	60–20	Room temp., in dark, few hours	116,49
Cibotium barometz L.	Woolly fern	Roots	20-5	25 minutes	114,48
Mammea suriga Buch-Ham	Ceylon ironwood	Roots	22	80°C	78,60
Bauhinia purpurea L.	Camel's foot	Leaves	50-20	Microwave, 30 sec	113,50
Terminalia arjuna Roxb	Arjun tree	Leaves	30-15	Room temperature	31,42
Betonica officinalis L.	Common hedge nettle	Flowers	10	80°C,24 hours	30,65
Lycium chinense Mill	Chinese wolfberry	Fruits	100-20	60°C, 75 seconds	26,38
Annona muricata	Graviola	Fruits	28-30	60°C, 5hours	93 ,61

Nanoscales of iron oxide and other metal oxides:

Iron oxide nanoparticles are used for cancer therapy, drug delivery, and damaged tissue therapy, and in labeling of the cells for monitoring the development of tumors, removing toxins from biological fluids, and magnetic resonance imaging (33, 37 and 51). Chromolaena odorata roots extract was used to synthesize Fe_3O_4NPs (29 and 110). The roots were washed with water and dried in the sun for 14 days, then 5g of root powder was added to 50 ml distilled water and the mixture heated at 85°C for 2 hours with Stirring continuously. The extract was then filtered and centrifuged to separate impurities. Iron salts were added to the plant extract and the mixture heated at 70°C. Iron oxide nanoparticles formations were observed within one hour, and electron microscope images indicated that the particles were spherical in shape, with dimensions in the range of 5.6-18.6 nanometers. Using (35 and 89) the aqueous extract of European corn fruits (Cornus mas L.) to manufacture nanoparticles is an easy, fast and economical way, and the resulting particles were spherical with diameters in the range of 20 - 40 nanometers. The iron oxide nanoparticles have a positive effect on increasing the biomass of the stems and roots of barley seedlings when watered at a concentration of 10 - 100 mg/L, and are commended by researcher fertilization. Other studies (32 and 92) used peels and palm seeds (Borassus flabellifer L.) to produce the nanoparticles which were, hexagonal in shape, with dimensions of about 35 nm. The aqueous extract of ginger roots was also used to produce nickel oxide nanoparticles of size 16-52 nm (40), and these particles had an inhibitory effect on the growth of staphylococcus aureus in the laboratory. Also (85) aqueous extract of Abbad sun seeds (Helianthus annuus L.) were used to produce manganese oxide particles with nanoscale of (10 - 70 nanometers). In another study, the extract from hydrolysis of Annona squamosal seeds were used in the synthesis of magnesium oxide nanoparticles which ranged in size from 27 to 86 nm (16 and 96). The aqueous extract of squash seeds (Cucurbita pepo L.) have also been used to produce titanium oxide nanoparticles (6 and 25).

Drug delivery:

The process of manufacturing a new drug is expensive and takes time, in addition to producing unfavorable results. As such researchers have resorted to working on the drugs themselves by changing their dosages, composition, and type of dose, as well as developing new drug delivery systems (13, 34, 43 and 44). Pregnant women are represented. Medicines are one of the important components used in new drug delivery systems. These carriers have entered the pharmaceutical field to achieve several goals, including increasing drug stability and bioavailability and preventing drug interactions. In the last three decades, different types of carriers have been developed for medicines such as cellular carriers, particulate carriers, lipoidal carriers, etc. These carriers differ from each other in terms of composition (11, 100 and 103), characteristics, and methods.

Anticancer properties:

Cancer can affect all human tissues derived from the epithelium. All types of carcinogenesis share a similar process, as they go through the same sequential stages from normal to hyperplasia, to site, and finally to metastatic or invasive carcinoma (63 and 75). Surgical resection alone is the cure for most cancers, but metastatic or invasive cancers cause more than 90% of cancer-related deaths (4 and 5). Biodegradable nanoparticles in the form of quantum spots have been used in the treatment of malignancies, with a reasonable surface change to immobilize both growths while concentrating substances and chemicals on their surfaces. Communications concerning insensitive cells and growth cells were imaged using a visual magnifying lens (7, 9 and 10). The speedy growth of this new science opens new opportunities as its uses show that nanotechnology will be among the main innovations of the 21st century (15, 17 and 24). In a new report, immune responses formed attractive poly (D, L-lactic-co-glycolic) (PLGA) nanoparticles with doxorubicin (DOX) adsorbed to concomitantly identify and treated malignant tumor growth. DOX and attractive nanoparticles were combined with PLGA nanoparticles, with DOX filling in as an anticancer medicine and Fe_2O_3 nanoparticles (12, 14 and

18). In addition, they used the Herceptin 1 antagonist to focus on malignant growths in the chest.

Conclusions

Delivery systems that have evolved for cancer treatment are, a challenge that usually presents opportunities in several fields of science, because of its great complexity. Innovative options are being investigated to make chemotherapy an effective treatment by targeting drugs to cancer cells through various modifications in delivery systems. As biopolymer produced from partial deacetylation and present in the exoskeleton of crustaceans and some insects as well as in the cell walls of many fungi. nanoparticles have specific solubility properties. The functional groups in its structure, crosslinking strength, affinity with other substances, biocompatibility, biodegradability, and mucosal adhesion, offer the bioavailability of a chemotherapeutic factor on cancer cells, without attacking healthy cells. This document compiled some interesting researches on using plant extracts with other biomedical materials to design, characterize, and develop novel delivery systems for chemotherapeutic factors, thereby enhancing the efficiency of therapying treating cancerous tumors.

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Author Contributions:

Author 1 writing—original draft preparation, Author 1 and Author 2 writing review and editing. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest:

The authors declare no conflict of interest.

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