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Plant-Based Calcium Fructoborate as Boron-Carrying Nanoparticles for Neutron Cancer Therapy

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Boron neutron capture therapy (BNCT) is an effective clinical method in cancer treatment based on fission reactions and nuclear capturing. In this method, use of the best boron-containing agents for boron therapy and boron delivery agent for transfer to the infectious site are the key points for efficient treatment. Our research indicated that calcium fructoborate(CF) was the best compound as a boron-containing agent for boron therapy. Furthermore, studies have demonstrated that liposomes can selectively and effectively deliver large quantities of boron to cells and that the compounds delivered by liposomes have a longer cell retention time. Indeed, liposomal encapsulation technology of CF as nanostructured liposome carriers (NLCs) was extensively evaluated due to the ability of these nano-vehicles for the delivery of boron compounds. In this work, the molecular composition of the CF used as a carrier supplement for cancer therapy is deeply investigated. FTIR, XRD, TG, DSC and Raman spectroscopic analyses were used for the characterization of the carrier. The experimental measurements agreed very well with the molecular formula of $Ca[(C_6H_{10}O_6)_2B]_{24}H_2O$.

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1. INTRODUCTION

In 1936, Locher realized the potential of neutron capture (NC) reaction with stable isotopes in the field of medicine, and subsequently Sweet suggested that the boron NC could be used to treat brain tumors [1]. After the initial discovery, several number of research groups throughout the world continued the early groundbreaking work of Sweet, Fairchild, and especially the pioneering clinical studies of Hatanaka in Japan [2, 3].

Boron neutron capture therapy (BNCT) was proposed for clinical treatment of cancer cells [4]. Recently, BNCT has used a number of ^{10}B-containing compounds to kill cancer cells selectively and also to treat the cancer via a cell-by-cell basis without affecting normal cells. The cancer cells are selectively destroyed using alpha and ^{7}Li particles which are generated by the $^{10}B(n,\alpha)^{7}Li$ reaction [5-13]. The $^{10}B(n,\alpha)^{7}Li$ nuclear reactions are demonstrated as follows:

$$^{10}B + n_{th}(0.025\ eV) \rightarrow [^{11}B]\begin{cases} ^{4}He + {}^{7}Li + 2.792\ MeV\ (6\%) \\ ^{4}He + {}^{7}Li + 2.310\ MeV\ (94\%) \\ {}^{7}Li + \gamma + 0.48\ MeV \end{cases} \quad (1)$$

^{10}B chemical compound which accumulates in the cancer cell is injected to a patient's body in advance. Usually, the evolution of the ^{10}B concentration in cancerous and healthy tissue is obtained indirectly from blood samples taken before, after and during the BNCT treatment.

It is possible that sufficient number of ^{10}B atoms (about 10^9 atoms/cell) will be selectively delivered to the cancer cells and enough thermal neutrons will be absorbed by the cancer cells to sustain a lethal $^{10}B(n,\alpha)\ ^{7}Li$-capture reaction [14]. In this article, the therapeutic effectiveness of each BNCT and IAEA standard modeling configuration for neutron beams were considered. Important parameters, including, $\varphi_{epithermal}/\varphi_{fast}$, $\varphi_{epithermal}/\varphi_{thermal}$, $\dot{D}_{fast}/\dot{D}_{epithermal}$, $\dot{D}_{\gamma}/\dot{D}_{epithermal}$ were often used for preliminary assessment.

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Owing to the cancer cells function, boron compounds do not enter easily and intact to cancer cells; but readily find their way into the targeted cells. Neutrons are irradiated on the affected part of the cancer, enabling selective destruction of the cancer cells containing boron by the alpha and lithium particles generated from the $^{10}B(n,\alpha)^{7}Li$ reaction.

Undoubtedly, this method is a biologically efficient and targeted method in radiation treatment [15]. Since the ionization range of both the α-rays and the ^{7}Li particles is short [~10 μm], the radiation damage occurs over a short-range and only the cancer cells are damaged and normal tissues can be spared. The treatment finishes in the irradiation for several times [16]. Quality of life (QOL) after the treatment is generally satisfaction.

Thus, modern BNCT is actually the combination of chemo and radiotherapy, which is used in the treatment of cancer cells. The great challenge of BNCT remains to bias the retention of ^{10}B toward cancer cells [17-20]. The selective target is a promising novelty in the field of cancer therapy. This specific Boron ray therapy is applied to cancer cells for the first time. Despite the usefulness and novelty of this strategic approach, boron carrier systems are required, as limiting the widespread application of the stated methodology. Indeed, in this study, for the development of the use of boron carrier systems, liposomal encapsulation of calcium fructoborate nanoparticles were considered as an appropriate substrate for anticancer boron compound and it was used as drug carrier system. This nano-conductor was designed to carry an anti-cancer carrier (calcium fructoborate) and its targeted release in cancer cells. In general, this is a novel approach that improves the performance, efficiency and also the quality of the clinical treatment.

Boron natural complexes are characterized as a boric acid ester with fructose, glucose, and sorbitol sugars [4, 5]. Because of molecular composition of calcium fructoborate (CF), it has recently been demonstrated to possess an interesting anti-oxidant compound [6], anti-inflammatory [7, 8] and anti-tumoral activities [9,10].

During the investigation on CF applicable behavior, it was found that liposomal encapsulation of CF is an interesting developement just introduced in the cancer therapy for boron supplementation. As a matter of fact, the structures of nano-liposomes and their use as drug delivery carriers are briefly reviewed in this article.

2. MATERIAL AND METHODS

2. 1. Preparation of CF For the synthesis of CF, Miljkovic's procedure was applied [21]. Based on the developed method, boric acid (Carlo Erba) was used. D-fructose was supplied by Sigma-aldrich and $CaCO_3$ and acetone were supplied by Merck. D-fructose (2.16 g) was dissolved in 10 ml of distilled water at room temperature, and 0.372 g boric acids was then added to this solution. Finally, 0.246 g calcium carbonate was added in small portions, under constant stirring. After the CO_2 evolution was stopped, 40 ml of acetone was added to the reaction mixture. The mixture was thoroughly agitated; then let it to be separated for equilibrium.

For separation of the two layers, the mixture was separated using a separation funnel. The lower oily layer, containing the crude boron complex was treated again with additional 40 ml of acetone. Following up next step, after one hour, crystallization was induced with a glass rod, and the oil slowly turned into a white crystalline solid. Finally, the product was filtered. The developed procedure and series of reactions for the synthesis of CF are illustrated in Figure 1. The proposed synthesis procedure, using CF as a precursor, marked as a quick and easy preparation method for the CF chain-like metaborate.

2. 2. Liposomal Encapsulation Technology Liposomes are small bubbles filled with water. The bubble is surrounded by water on the outside and filled with nano-drug inside. Moreover, their membranes are consisted of phospholipid bilayers.

There are various types of liposomes and methods for cancer therapy. The most important feature of liposomes is the fact that their phospholipid membrane is actually the same as the membrane of cells in the body. Active content is encapsulated into a liposome for improved protection, delivery, absorption, and bioavailability. Ultimately, the entrapment of the nano-drug is accomplished by the liposomal encapsulation technology (LET). Undeniably, LET represents a step forward approach in the delivery of carrier systems. Undoubtedly, a highly effective method is use of nanotechnologies to increase the efficiency of boron-containing absorption agent for boron therapy. Recently, there have been many efforts to demonstrate these nanostructures as carriers for drug release in human studies.

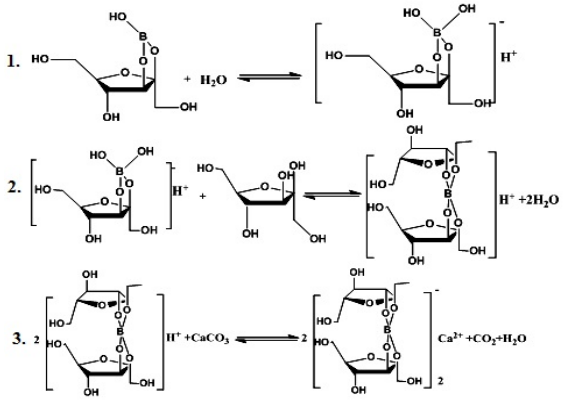

Figure 1. Procedure for the synthesis of calcium fructoborate

Some advantages of encapsulating ability of CF nano-liposomes are as follows: (1) low unwanted side effects, (2) low toxicity and (3) high efficiency.

This article describes the application of phosphatidylcholine for liposome developement. PEG has the advantage of increasing circulation lifetime of the liposomes. In addition, inclusion of PEG-ligand (for example: folate) is used to reduce aggregate formation [13]. Thus, both yield and injectability of complexes are enhanced. Scheme of nano-liposomal encapsulation of CF is demonstrated in Figure 2. Result demonstrated that particle size of nano-liposome encapsulated CF was 96 nm.

3. RESULTS AND DISCUSSION

3. 1. Quantitative Analysis Chemical analyses are designed to determine the amounts or proportions of the components of a substance.

3. 1. 1. FTIR and Raman Spectroscopic Studies Borate formation was confirmed by the FTIR spectra, Raman spectra and XRD analysis of the residue. FTIR is often used to find functional groups of organic substances and chemical bonds. Figure 3 shows FTIR peaks for CF, fructose, boric acid and calcium carbonate.

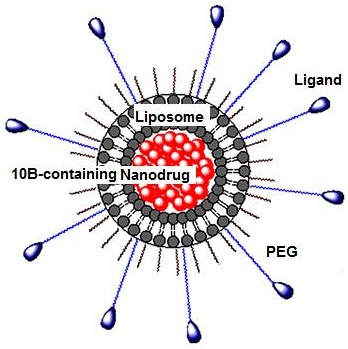

Figure 2. Liposomal encapsulation of calcium fructoborate

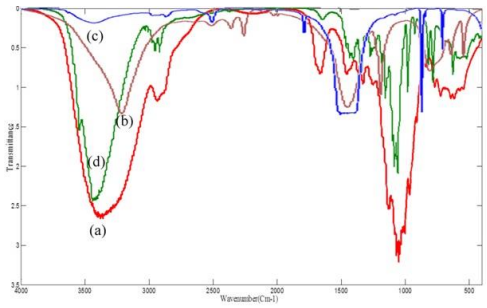

Figure 3. FTIR spectra of the prepared (*a*) calcium fructoborate, (b) boric acid, (c) calcium carbonate, and (d) fructose

In the transmission spectrum of CF, the vibrational broad band of fructose is found at 1100 cm^{-1} is. The intensity of the beaks compared with previously reported spectral information and complements in certain aspects were reduced by the new interactions in the CF molecule. The very strong band observed at 1444 cm^{-1} with a shoulder at 1497 cm^{-1} originates in B-O stretching attributed to the external O-atoms. The other very strong absorption peak found at 1200 cm^{-1} is related to B-O chain stretching. The remaining characteristic peak appeared in the FTIR spectrum exhibited in Figure 3 (773 (shoulder), 739 (strong), 712 (shoulder), 688 (very strong) and 643 (strong) cm^{-1}) are related to different deformational modes.

Raman spectrum is a sensitive probe for the study of biological materials with different electronic band structures depending on the number of layers. Raman spectroscopic analysis for fructose, boric acid, calcium carbonate and CF in the wave number range of 400-4000 cm^{-1} was performed and the results are presented in Figure 4. Raman spectra werere corded with a laser source, which was used at 532 nm with an average power of 64 mW. The spectra were recorded at an exposure time of 10 min and room temperature. With this technique, valuable information is obtained about the chemical composition, the secondary structure present in the macromolecules and the chemical surrounding of specific subunits. A major disadvantage of the Raman technique is the small scattering cross-section of biological molecules. As a result, high concentrations must be used. The Raman spectra data indicate a strong contribution from several bands for fructose associated with the O-H···O out-of-plane bending motions. The spectra of boric acid and calcium carbonate are very similar. The differences in the Raman spectra are not significant.

The movements of the Raman peak positions for CF were obviously presented. However, the peak at 3314 cm^{-1} presented in the Raman spectrum of CF is due to B-O bond. The B-O bond is broaden by the weak peaks from 1602 to 1471 cm^{-1}, according to the water crystallization of the structure.

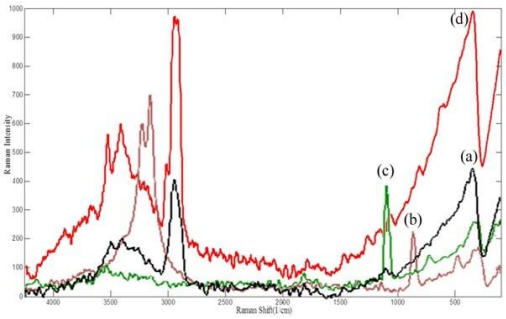

Figure 4. Raman spectroscopic analysis for (*a*) calcium fructoborate, (b) boric acid, (c) calcium carbonate and (d) fructose in the wave number range of 400-4000 cm^{-1}

3. 1. 2. X-rays Diffraction Analysis A XRD analysis for fructose, boric acid, calcium carbonate and CF was performed and the results are presented in Figure 5 (*a*)-(d). The XRD spectrum of the CF nanoparticles showed that they have an average diameter size of 16 nm. The results, matched exactly with that of the previous reports for CF.

Also, results demonstrated that the XRD patterns of these samples are very characteristic which only show the typical reflections of CF. Furthermore, fructose represents approximately 76% of the total mass of the complex and likely influences its crystalline structure. Indeed, when comparing diffraction peaks of fructose to the ones of crystallized CF, similarities in $2\theta = 16.86^{o}$, 19.92^{o} and 28.14^{o} can be identified.

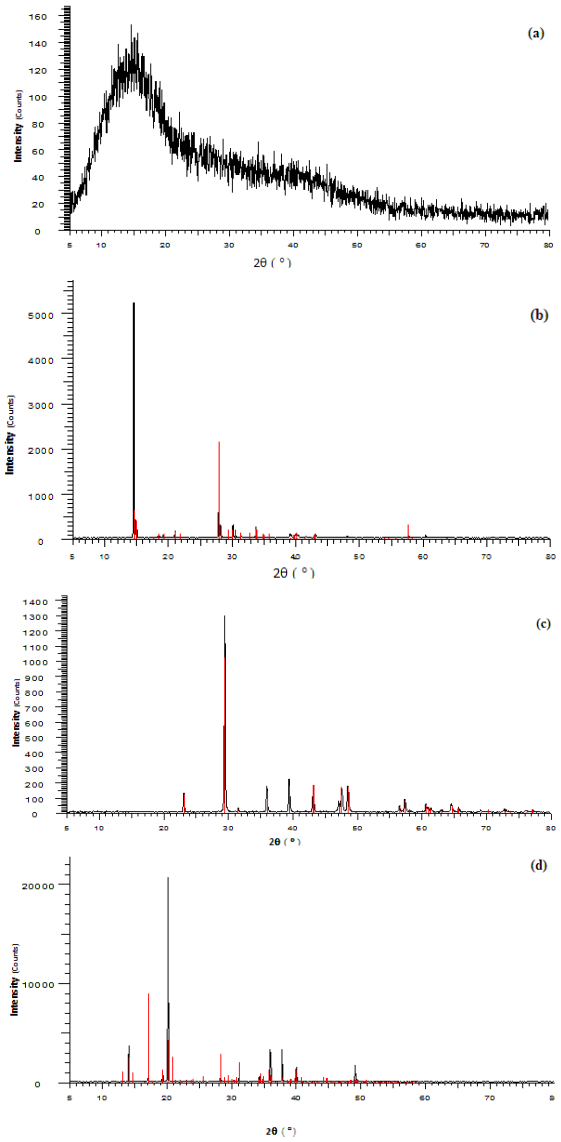

Figure 5. XRD patterns for (*a*) CF, (b) boric acid, (c) calcium carbonate and (d) fructose

The diffraction maxima of free fructose was not identified in the XRD spectrum of CF. For calcium carbonate and boric acid there were not identified; maximal values of the X-rays diffraction were in common with those of CF.

3. 1. 3. Thermal Analysis Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA) were performed in oxygen flow of 50 ml/min and at a heating rate of 5 °C/min. Sample quantities ranged between 10 and 20 mg. The obtained thermograms are shown in Figure 6. As can be seen in this figure, there is an endothermic peak about 120 °C indicating the hydration of water, and along with this process a very weak DSC endothermal signal occurred at 67 °C. There are also small exothermic peaks in the DSC curve of CF above 300 ºC. As can be seen in Figure 6, TGA curve consisted of three parts located between 120 and 240 °C, 240 and 420 °C and 420 and 600 °C.

These thermal degradation steps were attributed to DSC peaks at 181 °C, 315 °C, and finally a strong step at 452 °C. The total experimental mass loss was about 84%. By correlation and elemental analysis of the thermo gravimetric results obtained from experimental data, we found that no traces of precursors were observed. Furthermore, the correct molecular formula of CF was correlated as $Ca[(C_6H_{10}O_6)_2B]_{24}H_2O$, which has two times more boron than those reported in the literature [22-24].

3. 2. Intelligent Drug Delivery Systems Using Neutron Accelerator Performing successful BNCT experiments needs a suitable neutron source. Important factors of the neutron beam are flux and energy that are very important in the selection of neutron source. In most centers this method is used for treatment, reactor is a neutron source, which according to characteristics of the reactor appropriate neutrons are very high. High cost of construction of a BNCT center using reactor indirectly caused seeking for other sources such as accelerator and radioisotope source directly that each has their own advantage and disadvantages [25-29].

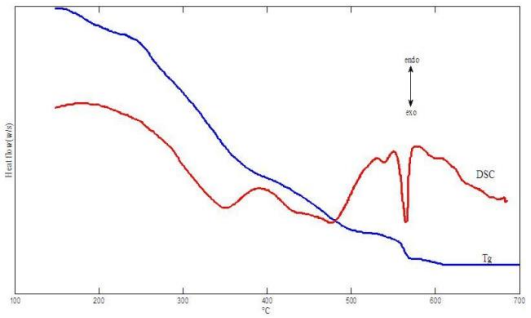

Figure 6. TG and DSC traces of the thermal decomposition of a calcium fructoborate sample

There are various types of neutron sources used for cancer therapy using nanostructured liposome carriers (NLCs) for drug delivery systems; but, all of these can be placed into two distinct categories based on the needed energy: nuclear reactor and/or accelerator. In order to remedy the cancer of 10 cm^2, 2×10^{13} neutrons and low energy are needed. Indeed, assuming a remedy time ~30 minutes, neutron flux $\Phi > 10^9$ n/(cm^2.s) are also needed.

Neutron accelerator has applications in medicine, security, and materials analysis. While passing through the tissue of the patient, the neutrons are slowed by collisions and become low energy thermal neutrons. Neutron accelerators are neutron source devices which contain compact linear accelerators and produce neutrons by fusing isotopes of hydrogen together. The fusion reactions take place in these devices by accelerating deuterium, tritium, or a mixture of these two isotopes into a metal hydride target which also contains deuterium, tritium or a mixture of these isotopes. Fusion of deuterium atoms (D + D) and a deuterium and a tritium atom (D + T) results in a He-3 and He-4 ions form, separately.Also, kinetic energy of neutrons is about 2.5 MeV and 14.1 MeV, respectively. In this research we have focused on the second method as a neutron source and Monte Carlo simulation. In addition, Pb and ^{238}U, Alf_3 and BeO were selected as neutron multipliers, moderator and reflector, respectively. Ultimately, the proposed epithermal neutron flux in suggested system is 10^9 n/cm^2.s which is a suitable flux for BNCT applications [30-34].

Based on IAEA standard modeling configuration for neutron beams [35] the α-particles and the ^7Li ions can destroy cells in mitosis. The challenge which may exist is to promote from experimental animal studies to clinical biodistribution studies, a step which has yet to be taken from experiment to clinical trials [36-40].

4. CONCLUSION

The BNCT is an innovative technique which has several advantages: as it is almost independent on the concentration and being a binary system technique both of the two components can be adjusted independently. This may lead to a wide range of research alternatives aimed to improve the technique; but still weak feasibility exists due to reactor source, large uncertainties in dosimetric measurements and protocols ^{10}B compound charging. The identified correct molecular formula of fructose was $Ca[(C_6H_{10}O_6)_2B]_2\cdot4H_2O$. Furthermore, CF is a biological product that can be used as boron carrier systems in human samples. Quantitative analysis of fructose, boric acid and calcium carbonate and CF showed that there are some similarities between their curves. In this research, there is a platform of liposomal encapsulation of CF as boron delivery agent that was designed and produced.

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6. REFERENCES

1. Locher, G.L., "Biological effects and therapeutic possibilities of neutrons", ***American Journal of Roentgenology*** Vol. 36, (1936), 1-13.
2. Sweet, W., Soloway, A. and Brownell, G., "Boron-slow neutron capture therapy of gliomas", ***Acta Radiologica: Therapy, Physics, Biology***, Vol. 1, No. 2, (1963), 114-121.
3. Hatanaka, H., Sweet, W., Sano, K. and Ellis, F., "The present status of boron-neutron capture therapy for tumors", ***Pure and Applied Chemistry***, Vol. 63, No. 3, (1991), 373-374.
4. Torres, N., Guevara-Cruz, M., Velázquez-Villegas, L.A. and Tovar, A.R., "Nutrition and atherosclerosis", ***Archives of Medical Research***, Vol. 46, No. 5, (2015), 408-426.
5. Rotaru, P., Scorei, R., Hărăbor, A. and Dumitru, M., "Thermal analysis of a calcium fructoborate sample", ***Thermochimica Acta***, Vol. 506, No. 1-2, (2010), 8-13.
6. Hakki, S.S., Malkoc, S., Dundar, N., Kayis, S.A., Hakki, E.E., Hamurcu, M., Baspinar, N., Basoglu, A., Nielsen, F.H. and Götz, W., "Dietary boron does not affect tooth strength, micro-hardness, and density, but affects tooth mineral composition and alveolar bone mineral density in rabbits fed a high-energy diet", ***Journal of Trace Elements in Medicine and Biology***, Vol. 29, (2015), 208-215.
7. Miljkovic, D., Miljkovic, N. and McCarty, M.F., "Up-regulatory impact of boron on vitamin d function–does it reflect inhibition of 24-hydroxylase?", ***Medical Hypotheses***, Vol. 63, No. 6, (2004), 1054-1056.
8. Iriti, M. and Varoni, E.M., Grape bioactives for human health, in Fruits, vegetables, and herbs. 2016, Elsevier.221-238.
9. Balakrishnan, B., Joshi, N., Jayakrishnan, A. and Banerjee, R., "Self-crosslinked oxidized alginate/gelatin hydrogel as injectable, adhesive biomimetic scaffolds for cartilage regeneration", ***Acta Biomaterialia***, Vol. 10, No. 8, (2014), 3650-3663.
10. Robbins, W.A., Xun, L., Jia, J., Kennedy, N., Elashoff, D.A. and Ping, L., "Chronic boron exposure and human semen parameters", ***Reproductive Toxicology***, Vol. 29, No. 2, (2010), 184-190.
11. Marone, P.A., Heimbach, J.T., Nemzer, B. and Hunter, J.M., "Subchronic and genetic safety evaluation of a calcium fructoborate in rats", ***Food and Chemical Toxicology***, Vol. 95, (2016), 75-88.

12. Novelle, M.G., Wahl, D., Dieguez, C., Bernier, M. and de Cabo, R., "Resveratrol supplementation: Where are we now and where should we go?", ***Ageing Research Reviews***, Vol. 21, (2015), 1-15.

13. Jose, S.K., George, A., Unnikrishnan, N., Joseph, C. and Biju, P., "Synthesis and photoluminescence characteristics of near white light emitting cab2o4: Dy3+, li+ phosphor", ***Journal of Physics and Chemistry of Solids***, Vol. 119, (2018), 166-174.

14. Caballero, B., Finglas, P. and Toldrá, F., "Encyclopedia of food and health, Academic Press, (2015).

15. Haghighatdoost, F. and Hariri, M., "Effect of resveratrol on lipid profile: An updated systematic review and meta-analysis on randomized clinical trials", ***Pharmacological Research***, Vol. 129, (2018), 141-150.

16. Militaru, C., Donoiu, I., Craciun, A., Scorei, I.D., Bulearca, A.M. and Scorei, R.I., "Oral resveratrol and calcium fructoborate supplementation in subjects with stable angina pectoris: Effects on lipid profiles, inflammation markers, and quality of life", ***Nutrition***, Vol. 29, No. 1, (2013), 178-183.

17. Pietrzkowski, Z., Hunter, J., Evers, B. and Pond, H., Plant borates and potential uses to promote post-training recovery and to mitigate overtraining syndrome, in Nutrition and enhanced sports performance. 2013, Elsevier.479-485.

18. Nielsen, F.H., "Update on human health effects of boron", ***Journal of Trace Elements in Medicine and Biology***, Vol. 28, No. 4, (2014), 383-387.

19. Nielsen, F.H., Nonessential trace minerals: Basic nutritional and toxicological aspects, in Molecular, genetic, and nutritional aspects of major and trace minerals. 2017, Elsevier.527-537.

20. Nikkhah, S., Dolatian, M., Naghii, M.R., Zaeri, F. and Taheri, S.M., "Effects of boron supplementation on the severity and duration of pain in primary dysmenorrhea", ***Complementary Therapies in Clinical Practice***, Vol. 21, No. 2, (2015), 79-83.

21. Miljkovic, D., *Boron carbohydrate complexes and uses thereof*. 1999, Google Patents.

22. Sahebkar, A., Serban, C., Ursoniu, S., Wong, N.D., Muntner, P., Graham, I.M., Mikhailidis, D.P., Rizzo, M., Rysz, J. and Sperling, L.S., "Lack of efficacy of resveratrol on c-reactive protein and selected cardiovascular risk factors—results from a systematic review and meta-analysis of randomized controlled trials", ***International Journal of Cardiology***, Vol. 189, (2015), 47-55.

23. Bhullar, K.S. and Udenigwe, C.C., "Clinical evidence of resveratrol bioactivity in cardiovascular disease", ***Current Opinion in Food Science***, Vol. 8, (2016), 68-73.

24. Raj, P., Louis, X.L., Thandapilly, S.J., Movahed, A., Zieroth, S. and Netticadan, T., "Potential of resveratrol in the treatment of heart failure", ***Life sciences***, Vol. 95, No. 2, (2014), 63-71.

25. Fantidis, J. and Antoniadis, A., "Optimization study for bnct facility based on a dt neutron generator", ***International Journal of Radiation Research,*** Vol. 13, No. 1, (2015), 13-24.

26. Guan, X., Murata, I. and Wang, T., "Performance verification of an epithermal neutron flux monitor using accelerator-based bnct neutron sources", ***Journal of Instrumentation***, Vol. 12, No. 09, (2017), P09013.

27. Sahoo, G., Sharma, S., Tripathy, S. and Bandyopadhyay, T., "Design and dosimetric evaluation of beam shaping assembly for bnct of compact d–t neutron generator by monte carlo simulation", ***Biomedical Physics & Engineering Express***, Vol. 4, No. 1, (2017), 015018.

28. Fantidis, J.G. and Nicolaou, G., "Optimization of beam shaping assembly design for boron neutron capture therapy based on a transportable proton accelerator", ***Alexandria Engineering Journal***, Vol. 57, No. 4, (2018), 2333-2342.

29. Torabi, F., Masoudi, S.F. and Rahmani, F., "Photoneutron production by a 25 mev electron linac for bnct application", ***Annals of Nuclear Energy***, Vol. 54, (2013), 192-196.

30. Briesmeister, J.F., "Mcnp-a general monte carlo code n-particle transport code version 4c", Los Alamos, NM: Los Alamos National Laboratory, LA-13709M, (2000).

31. Eskandari, M. and Kashian, S., "Design of moderator and multiplier systems for d–t neutron source in bnct", ***Annals of Nuclear Energy***, Vol. 36, No. 8, (2009), 1100-1102.

32. Cerullo, N., Esposito, J. and Leung, K., "Irradiation facility for boron neutron capture therapy application based on a rf-driven d–t neutron source and a new beam shaping assembly", ***Review of Scientific Instruments***, Vol. 73, No. 2, (2002), 938-938.

33. Tanaka, K., Kobayashi, T., Bengua, G., Nakagawa, Y., Endo, S. and Hoshi, M., "Characterization of moderator assembly dimension for accelerator boron neutron capture therapy of brain tumors using neutrons at proton energy of", ***Medical Physics***, Vol. 33, No. 6Part1, (2006), 1688-1694.

34. Baba, M., Unno, Y., Nakamura, T., Yonai, S., Tahara, Y. and Yokobori, H., "Design and benchmark experiment of cyclotron-based neutron source for bnct", in Abstracts of the Second Asian and Oceanic Congress for Radiation Protection., (2006).

35. Fantidis, J., "Beam shaping assembly study for bnct facility based on a 2.5 mev proton accelerator on li target", ***Journal of Theoretical and Applied Physics***, Vol. 12, No. 4, (2018), 249-256.

36. Nasri, H., Sahinfard, N., Rafieian, M., Rafieian, S., Shirzad, M. and Rafieian-Kopaei, M., "Turmeric: A spice with multifunctional medicinal properties", ***Journal of HerbMed Pharmacology***, Vol. 3, (2014), 5-8.

37. Bitar, A., Ahmad, N.M., Fessi, H. and Elaissari, A., "Silica-based nanoparticles for biomedical applications", ***Drug Discovery Today***, Vol. 17, No. 19-20, (2012), 1147-1154.

38. Thakor, A.S. and Gambhir, S.S., "Nanooncology: The future of cancer diagnosis and therapy", ***CA: a Cancer Journal for Clinicians***, Vol. 63, No. 6, (2013), 395-418.

39. Davis, M.E., Chen, Z. and Shin, D.M., Nanoparticle therapeutics: An emerging treatment modality for cancer, in Nanoscience and technology: A collection of reviews from nature journals. 2010, World Scientific.239-250.

40. Peer, D., Karp, J.M., Hong, S., Farokhzad, O.C., Margalit, R. and Langer, R., "Nanocarriers as an emerging platform for cancer therapy", ***Nature Nanotechnology***, Vol. 2, No. 12, (2007), 751-760.

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Liposome Encapsulation

چکیده

روش درمان با گیر انداختن نوترون در بور (BNCT) یکی از روش های موثر در درمان سرطان بر اساس واکنش های همجوشی و تسخیر هسته ای است. در این روش، استفاده از بهترین ماده حاوی بور به منظور درمان به روش بور و انتخاب بهترین عامل حامل بور به منظور انتقال آن به جایگاه عفونت، از نکات کلیدی به منظور یک درمان موثر است. تحقیقات ما نشان داد که ترکیب کلسیم فروکتوبورات (CF) بهترین ترکیب به عنوان یک ماده حاوی بور برای بور درمانی است. علاوه بر این، مطالعات نشان داده است که لیپوزوم ها می توانند به طور موثر و انتخابی مقادیر زیادی از بور را به سلول ها منتقل کنند و ترکیباتی که توسط لیپوزوم ها منتقل می شوند، می توانند مدت زمان طولانی تری در سلول ها بمانند. در واقع، تکنولوژی کپسول سازی لیپوزومی CF به علت توانایی این نانووسیله در انتقال ترکیبات حاوی بور به عنوان یک نانوساختار حامل لیپوزومی (NLCs) به طور گسترده ای مورد بررسی قرار گرفته است. در این مقاله، ترکیب مولکولی CF که به عنوان یک عامل رسانش جایگزین برای درمان سرطان مورد استفاده قرار گرفته است، به طور گسترده مورد بررسی قرارگرفته است. تجزیه و تحلیل اسپکتروسکوپی FT-IR، XRD، TG، DSC و رامان اسپکتروسکوپی برای تشخیص ساختار ترکیب حامل بور انجام شده است. اندازه گیری های تجربی با دقت بسیار خوبی فرمول مولکولی $Ca([C_6H_{10}O_6]2B)24H_2O$ را برای ساختار موردنظر تایید نموده اند.

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