Nutraceutical Concepts and Dextrin-Based Delivery Systems

Subjects: Nanoscience & Nanotechnology

Contributor: Gjylije Hoti , Adrián Matencio , Alberto Rubin Pedrazzo , Claudio Cecone , Silvia Lucia Appleton , Yousef Khazaei Monfared , Fabrizio Caldera , Francesco Trotta

Nutraceuticals are natural bioactive or chemical compounds acclaimed for their valuable biological activities and health-promoting effects. The global community is faced with many health concerns such as cancers, cardiovascular and neurodegenerative diseases, diabetes, arthritis, osteoporosis, etc. The effect of nutraceuticals is similar to pharmaceuticals, even though the term nutraceutical has no regulatory definition. The usage of nutraceuticals, to prevent and treat the aforementioned diseases, is limited by several features such as poor water solubility, low bioavailability, low stability, low permeability, low efficacy, etc. These downsides can be overcome by the application of the field of nanotechnology manipulating the properties and structures of materials at the nanometer scale.

disease nutraceuticals nano-carrier starch linear dextrin cyclic dextrin nanosponges drug delivery nutraceutical delivery

1. Introduction

Nutraceuticals are natural bioactive or chemical compounds acclaimed for their valuable biological activities and health-promoting effects [1][2][3]. The usage of nutraceuticals, to prevent and treat many health concerns, is limited by several features such as poor water solubility, low bioavailability, low stability, low permeability, low efficacy, etc. The field of nanotechnology is applied to overcome the aforementioned downsides by manipulating the properties and structures of materials at the nanometer scale [4]. The synthesis, characterization, and applications of dextrin-based nano delivery systems are explored to enable the successful development of nutraceutical delivery systems (**Figure 1**).

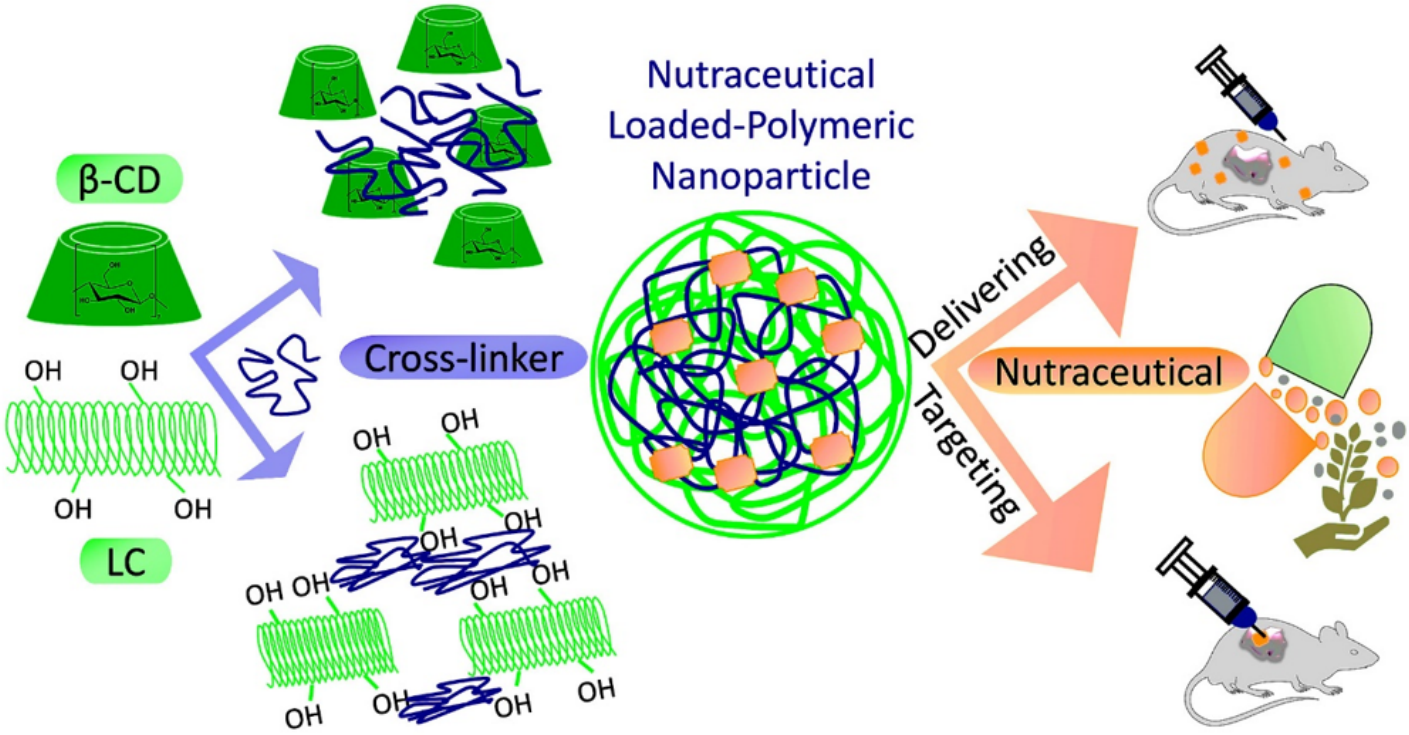

Figure 1. Overview of dextrin-based chemically cross-linked hydrogels as the most biocompatible and natural system to deliver nutraceuticals.

The industrialization and changing work cultures have caused numerous air and water pollutions, soil, and food contamination because of the extensive use of various harmful man-made items such as chemicals, heavy metals, electromagnetic waves, etc. Economic development has drastically changed human lifestyles because of the fast-eating cultures with decreasing nutrient quality. The nutritional deficiencies have caused various diseases such as diabetes, obesity, various cancers, neurodegenerative diseases, heart diseases, physiological problems, hypertension and dyslipidemia, chronic and vascular diseases, osteoporosis, arthritis, etc [5][6][7][8]. There are a few challenges to defining the health benefits of certain foods, improving immune function, preventing specific diseases, and reducing side effects, and health care costs. Throughout the years, the major concern of humankind around the world has been the research, development, and commercialization of nutraceuticals, functional food ingredients, and dietary supplements. Bioavailability, biocompatibility, solubility, loading efficacy, toxicity, the release, the activity, and the pharmacokinetics (PKs) of the drugs, etc., are the requirements to achieve a higher therapeutic purpose [1][7][9][10][11].

2. Nutraceuticals

Nutraceuticals are natural or chemical bioactive compounds that possess valuable biological activities and demonstrated physiological benefits. They offer promotion of the body's natural healing, prevention, and treatment of the disease [1][2][3]. Certain organizations proposed several definitions for nutraceuticals, as one of the most active areas of research with a deficiency of a favorable regulatory environment.

"A substance that is cultivated/produced/extracted or synthesized under optimal and reproducible conditions and when administered orally to patients, would provide the nutrient required for bringing altered body structure and function back to normal, thus improving the health and wellbeing of the patients", is the most appropriate definition for nutraceuticals [10]. The movement of nutraceuticals in the global market is "unstoppable" [12]. Nutraceuticals can be classified into broad classes based on food bioavailability, mechanism of action, and chemical nature [13][14]. Regarding the food source, nutraceuticals can be divided into traditional and non-traditional [15]. Based upon nutraceutical chemical nature, more specifically upon functional groups, there are comprised several large groups such as isoprenoid derivatives, phenolic substances, fatty acids, structural lipids, carbohydrate derivatives, amino acid derivatives, microbes, and minerals, which provide a basis for subclassification [13][16][17]. Concerning specific therapeutic properties, nutraceuticals are known for anti-inflammatory, anti-microbial, anti-oxidant, anti-hypercholesterolemic, anti-aggregate, anti-hypertensive, anti-carcinogenic, osteogenetic, or bone protective properties, etc.

3. Delivery systems for nutraceuticals

Nanotechnology is advantageous for manipulating the properties and structures of materials at the nanometer scale and therefore has opened up new opportunities for numerous applications in biotechnology, molecular biology, medicine, environmental science, etc [4]. The field of nanotechnology, through the efficacy of nano-drug delivery systems, contributes to every walk of life improving the bioavailability, biocompatibility, solubility, drug loading efficacy, and surface modifications of bioactive and chemical molecules [18]. The application of nanotechnology in health care is extensively adopted as a robust driver of biomedical novelty [19].

- Dextrin

Dextrin is one of the most noteworthy polymers because of its various features such as hygroscopicity, fermentability, sweetness, stability, gelation, solubility, bioavailability, and molecular compositions. Dextrin is a low-molecular-weight carbohydrate produced by enzymatic and/ or acid partial hydrolysis of starch, with the same general formula as starch but smaller and less complex. It contains α-(1→4) D-glucose units of amylose and the α-(1→4) and α-(1→4,6)-D-glucose units of amylopectin with lower polymerization. During the enzymatic degradation of starch, linear and cyclic dextrins are formed [20][21][22][23][24]. Dextrins are widely used in a variety of applications such as adhesive in the manufacture of textiles, cosmetics, gummed tapes, and paper, biomedical, and pharmaceutical applications [22]. Because dextrins are easily degraded by α-amylase, the chemical modification can tailor the dextrin structure for satisfying a variety of drug delivery objectives [25]. The native starches are often modified as a consequence of several unfavorable properties such as high hydrophilicity, poor solubility, etc. The chemical modification means the introduction of functional groups to the molecule of starch giving characteristic properties [26][27][28]. Among dextrins, cyclodextrin (CD) modifications have become a major area of interest for numerous investigations and, therefore they are widely explored as drug delivery systems.

- Dextrin-based polymers as delivery systems matrices

Cyclodextrins (CDs) are cyclic oligosaccharides produced via cyclodextrin (CD)- glycosyltransferase from starch, by certain microbes such as Bacillus macerans. CDs contain six (αCD), seven (βCD), eight (γCD), or more (α-1,4)-

linked α-D-glucopyranose units. The truncated shape of CDs is because of the chair conformation of glucopyranose units with the hydroxyl groups orientated to the cone exterior. The primary hydroxyl groups of the sugar residues are at the narrow edge of the cone, and the secondary hydroxyl groups are at the wider edge [29]. CDs tend to form inclusion complexes because of their lipophilic interior and hydrophilic exterior [30][31]. Even though the unique structure of CDs has fascinated scientists around the world, native CDs are appropriate only for the molecule recognition of a wide range of substrates. Moreover, they have various limitations such as the inability of including certain hydrophilic compounds or high molecular-weight drugs, low aqueous solubility, and toxicity in the case of β-CD when administered intravenously [32][33][34]. Therefore, specific applications require overcoming the aforesaid limitations by chemical modifications of CD structures [32][35].

In CDs, hydroxyl groups can be modified by replacing the hydrogen atom or the hydroxyl group with a variety of substituting groups [27]. CD derivatives and CD-based polymers appear as a powerful tool. CD derivatives comprise the randomly methylated β-CD, the hydroxypropyl derivatives of β- and γ-CD, sulfobutylether β-CD, and the branched CDs [36], whereas CD-based polymers, containing two or more covalently linked CD-units, can be water-soluble and moderately swelling or insoluble and strongly swelling [37]. CD-based nanosponges (NSs) can easily be obtained by reacting the nucleophilic hydroxyl group of the selected CD with a suitable cross-linking reagent, containing two electrophilic sites, that convert molecular nanocavities into insoluble three-dimensional, nanoporous structures. Widely-used cross-linkers that influence the behavior of the CD units are epichlorohydrin for hydrophilic NSs synthesis, and diphenyl carbonate (DPC), pyromellitic dianhydride (PMDA), diisocyanates, carbonyldiimidazole (CDI) for hydrophobic NSs synthesis. With a highly porous nanomeric and insoluble nature, CD-NSs are capable of encapsulating a variety of substances, particularly of increasing the solubility of poorly water-soluble drugs, prolonging their release, and improving their bioavailability and stability. Because of these characteristics and their harmlessness, CD-based NSs are used in certain fields such as chemistry, gene delivery, agriculture, cosmetics, food, biomedicine, biotechnology, biocatalysis, etc. However, the main area of investigation so far is the pharmacy, in which CD-NSs have been proposed as drug delivery systems [30][31][38][39][40][41][42][43][44]. Therefore, it is no wonder that the demand and the need for an explosive scientific and technological revolution have increased over the years.

Developing effective CD-based systems that can improve the properties of the nutraceutical has been attractive for many applications, particularly in the field of pharmaceuticals as delivery systems. CD-based nanosponges (NSs) appear as advanced drug carriers and, therefore, can also contribute as nutraceutical carriers. The history of CD-NSs, detailed by Krabicovà et al., over years has experienced significant progress. According to the chemical composition and properties, CD-NSs with particular attention to the pharmaceutical field can be divided into four generations, as overviewed by Caldera et al. The CD-NSs have evolved from the plain NSs to modified NSs, stimuli-responsive CD polymers, and molecularly imprinted CD-based polymers (MIPs-CD). The first generation of CD-NSs remains among the most commonly explored NSs as drug delivery systems. This generation comprises urethane (or carbamate), carbonate, ester, and ether CD-NSs. Delivery challenges for each native CD have been addressed through the CD-NSs generations which have improved the delivery kinetics for most of the therapeutic agents. CD-NSs are well-known delivery systems of several nutraceuticals such as quercetin [45], curcumin [46], resveratrol [47], thyme essential oil [48], melatonin [49], etc. Maltodextrin is defined as a hydrolyzed starch product [32]

consisting of D-glucose units linked primarily by α (1,4)-glycosidic bonds [50]. Maltodextrins are classified by their values of dextrose equivalent (DE). The DE ranges up to 20 and expresses the number of reducing sugars present in the polymer [51][52][53]. Thanks to the helical structure of the amylose chains, maltodextrins can act as complexing agents demonstrating a strategy to integrate drug-loaded carriers into hydrogels for drug delivery and tissue engineering applications [54]. The researchers still lack deeper knowledge of the forces involved in the complex formation of maltodextrins with nutraceuticals, and of their pharmaceutical applications.

4. Concluding Remarks

Nutraceuticals are considered to act against various nutritionally induced diseases such as obesity, cancers, diabetes, neurodegenerative diseases, cardiovascular disease, allergy, respiratory disorders, arthritis, etc. Nutraceuticals are considered a powerful instrument to facilitate lifespan, optimal health, and quality of life. The health benefits of the nutraceuticals are limited by the low bioavailability, low efficacy, low aqueous solubility, degradation and metabolism, and epithelial permeability.

This research shows the use of dextrin-based chemically cross-linked polymer as the most preferred, advanced, biocompatible, and natural system to deliver nutraceuticals.

One of the most commonly studied systems is cyclodextrin (CD)-based nanosponges (NSs). Due to their highly porous nanomeric nature, CD-NSs are found in different applications ranging from chemistry, pharmacy, biomedicine, gene delivery, food and biotechnology, environment, etc.

CD-NSs are efficient encapsulating agents for delivering nutraceuticals with controlled kinetics through the topical, oral, and parenteral routes. The nanomaterials based on CD-NSs, in contrast to free nutraceuticals and native dextrin units, improved the solubility, biocompatibility, bioavailability, encapsulation, and release capacity of the nutraceuticals, and therefore are considered the most effective delivery systems. Numerous nanomaterials-based drug delivery systems, as the most advanced approach contributing to every walk of life, have been prepared. Although maltodextrins are known for a higher aqueous solubility and are less expensive than CDs, their modified forms need to be further studied in pharmaceutical applications. Therefore, the extensive literature about the synthesis, characterization, and applications of the modified CDs, will fully instruct the modified linear dextrins. It can be forecasted that the more advanced nanoparticle drug delivery systems will be released and overtake the market.

References

1. Zhao J. Nutraceuticals, Nutritional Therapy, Phytonutrients, and Phytotherapy for Improvement of Human Health: A Perspective on Plant Biotechnology Application. Recent Pat Biotechnol. 2007;1:75-97. doi:10.2174/187220807779813893.

2. Andlauer W, Fürst P. Nutraceuticals: A piece of history, present status and outlook. Food Res Int. 2002;35:171-176. doi:10.1016/S0963-9969(01)00179-X.
3. Shahidi F. Nutraceuticals, functional foods and dietary supplements in health and disease. J Food Drug Anal. 2012;20:226-230. doi.org/10.38212/2224-6614.2144.
4. Kumar S, Nehra M, Kedia D, Dilbaghi N, Tankeshwar K, Kim K-H. Nanotechnology-based biomaterials for orthopaedic applications: Recent advances and future prospects. Mater Sci Eng C. 2020;106:1-25. doi:10.1016/j.msec.2019.110154.
5. Prabu S, Suriyaprakash TK, Kumar C, Kumar S. Nutraceuticals and their medicinal importance. Int J Heal Allied Sci. 2012;1(2):7. doi:10.4103/2278-344x.101661.
6. Pandey M, Verma RK, Saraf SA. Nutraceuticals: New era of medicine and health. Asian J Pharm Clin Res. 2010;3(1):4. ISSN 0974-2441.
7. Prabu SL, Suriyaprakash TNK, Kumar CD, Sureshkumar S, Ragavendran T. Nutraceuticals : A review. Elixir Pharm. 2012;46:8372-8377. ISSN: 2229-712X.
8. Das L, Bhaumik E, Raychaudhuri U, Chakraborty R. Role of nutraceuticals in human health. J Food Sci Technol. 2012;49(2):173-183. doi:10.1007/s13197-011-0269-4.
9. Shahidi F. Nutraceuticals and functional foods: Whole versus processed foods. Trends Food Sci Technol. 2009;20:376-387. doi:10.1016/j.tifs.2008.08.004.
10. C. Gupta R. Nutraceuticals: Efficacy, Safety and Toxicity. (C. Gupta R, ed.). Elsevier Inc.; Amsterdam, The Netherlands, 2016; ISBN: 9780128021477.
11. Shekhar V, Jha AK, Dangi JS. Nutraceuticals: A Re-emerging Health Aid. In: International Conference on Food, Biological and Medical Sciences (FBMS-2014). ; 2014:105-107. doi:10.15242/iicbe.c0114536.
12. Brower V. Nutraceuticals: Poised for a healthy slice of the healthcare market? Nat Biotechnol. 1998;16:728-731. doi: 10.1038/nbt0898-728.
13. Chanda S, Tiwari RK, Kumar A, Singh K. Nutraceuticals inspiring the current therapy for lifestyle diseases. Adv Pharmacol Sci. 2019:5. doi:10.1155/2019/6908716.
14. Ali A, Ahmad U, Akhtar J, Badruddeen, Khan MM. Engineered nano scale formulation strategies to augment efficiency of nutraceuticals. J Funct Foods. 2019;62:16. doi:10.1016/j.jff.2019.103554.
15. Bhaskarachary K, Vemula SR, Gavaravarapu SRM, Joshi AKR. Traditional foods, functional foods and nutraceuticals. Proc Indian Natl Sci Acad. 2016;82(5):1565-1577. doi:10.16943/ptinsa/2016/48888.
16. Ghosh D, Bagchi D, Konishi T. Clinical Aspects of Functional Foods and Nutraceuticals. CRC Press, Taylor&Francis Group; 2015. doi:10.1201/b17349.

17. Wildman REC. Nutraceuticals and Functional Foods. In: Handbook of Nutraceuticals and Functional Foods. 3d Edition. CRC Press, Taylor&Francis Group; Boca Raton, FL, USA, 2020; ISBN: 9781498703727.
18. Pillai SC, Borah A, Jacob EM, Kumar DS. Nanotechnological approach to delivering nutraceuticals as promising drug candidates for the treatment of atherosclerosis. Drug Deliv. 2021;28(1):550-568. doi:10.1080/10717544.2021.1892241.
19. Lidia A-V, Carlos Z-M, Alicia R-M, Amalia V, Jose V-B. Nutraceuticals: definition, applied nanoengineering in their production and applications. Int J Biosens Bioelectron. 2019;5(3):56-61. doi:10.15406/ijbsbe.2019.05.00154.
20. Das D, Pal S. Modified biopolymer-dextrin based crosslinked hydrogels: application in controlled drug delivery. RSC Adv. 2015;5:25014-25050. doi:10.1039/c4ra16103c.
21. Carvalho J, Gonçalves C, Gil AM, Gama FM. Production and characterization of a new dextrin based hydrogel. Eur Polym J. 2007;43:3050-3059. doi:10.1016/j.eurpolymj.2007.02.046.
22. Gonçalves C, Moreira SM, Carvalho V, Silva DM, Gama M. Dextrin. Encycl Biomed Polym Polym Biomater. 2016:2634-2649. doi:10.1081/e-ebpp-120050698.
23. Silva DM, Nunes C, Pereira I, et al. Structural analysis of dextrins and characterization of dextrin-based biomedical hydrogels. Carbohydr Polym. 2014;114:458-466. doi:10.1016/j.carbpol.2014.08.009.
24. Klein S. Polysaccharides in Oral Drug Delivery - Recent Applications and Future Perspectives. In: ACS Symposium Series. ; 2009:13-30. doi:10.1021/bk-2009-1017.ch001.
25. Hreczuk-Hirst D, Chicco D, German L, Duncan R. Dextrins as potential carriers for drug targeting: tailored rates of dextrin degradation by introduction of pendant groups. Int J Pharm. 2001;230:57-66. doi: 10.1016/s0378-5173(01)00859-6.
26. Alcázar-Alay SC, Meireles MAA. Physicochemical properties, modifications and applications of starches from different botanical sources. Food Sci Technol. 2015;35(2):215-236. doi:10.1590/1678-457X.6749.
27. Lewicka K, Siemion P, Kurcok P. Chemical Modifications of Starch: Microwave Effect. Int J Polym Sci. 2015:1-10. http://dx.doi.org/10.1155/2015/867697.
28. Haq F, Yu H, Wang L, et al. Advances in chemical modifications of starches and their applications. Carbohydr Res. 2019;476:12-35. doi:10.1016/j.carres.2019.02.007.
29. Brewster ME, Loftsson T. Cyclodextrins as pharmaceutical solubilizers. Adv Drug Deliv Rev. 2007;59(7):645-666. doi:10.1016/j.addr.2007.05.012.
30. Ali Osmani Riyaz; Kulkarni Parthasarathi; Manjunatha Shringari; Gowda Vishakante; Hani Umme; Vaghela Rudra; and Bhosale Rohit. Chapter 9 Cyclodextrin Nanosponges in Drug Delivery and

Nanotherapeutics. In: Lichtfouse Eric, Dasgupta Nandita RS, ed. Environmental Nanotechnology. Springer; 2018:405. doi:https://doi.org&10.1007/978-3-319-76090-2.

31. Sherje AP, Dravyakar BR. Cyclodextrin-based nanosponges: A critical review. Carbohydr Polym. 2017;173:37-49. doi:10.1016/j.carbpol.2017.05.086.
32. Stella J. Valentino; Rajewski A. Roger; Cyclodextrins: Their Future in Drug Formulation and Delivery. Pharm Res. 1997;Vol. 14, N:11. doi:10.1023/a:1012136608249.
33. Rousseau J, Menuel S, Rousseau C, Hapiot F, Monflier E. Cyclodextrins as Porous Material for Catalysis. Elsevier Inc.; 2016. doi:10.1016/B978-0-12-801713-5.00002-1.
34. Hedges AR. Industrial applications of cyclodextrins. Chem Rev. 1998;98(5):2035-2044. doi:10.1021/cr970014w.
35. Sun J, Zhao R, Zeng J, Li G, Li X. Characterization of Destrins with Different Dextrose Equivalents. Molecules. 2010;15(8):5162-5173. doi:10.3390/molecules15085162.
36. Jambhekar SS, Breen P. Cyclodextrins in pharmaceutical formulations I: structure and physicochemical properties, formation of complexes, and types of complex. Drug Discov Today. 2016;21:356-362. doi:10.1016/j.drudis.2015.11.017.
37. Bekers O, Uijtendaal E V., Beijnen JH, Bult A, Underberg WJM. Cyclodextrins in the pharmaceutical Field. Drug Dev Ind Pharm. 1991;17(11):1503-1549. doi:10.3109/03639049109026630.
38. Chilajwar S V, Pednekar PP, Jadhav KR, Gupta GJ, Kadam VJ. Cyclodextrin-based nanosponges: a propitious platform for enhancing drug delivery. Expert Opin Drug Deliv. 2014;11(1):111-120. doi:10.1517/17425247.2014.865013.
39. Berto S, Bruzzoniti MC, Cavalli R, et al. Synthesis of new ionic β-cyclodextrin polymers and characterization of their heavy metals retention. J Incl Phenom Macrocycl Chem. 2007;57(1-4):631-636. doi:10.1007/s10847-006-9273-0.
40. Zhang D, Lv P, Zhou C, Zhao Y, Liao X, Yang B. Cyclodextrin-based delivery systems for cancer treatment. Mater Sci Eng C. 2019;96(April):872-886. doi:10.1016/j.msec.2018.11.031.
41. Swaminathan S, Vavia PR, Trotta F, Cavalli R. Nanosponges encapsulating dexamethasone for ocular delivery: Formulation design, physicochemical characterization, safety and corneal permeability assessment. J Biomed Nanotechnol. 2013;9(6):998-1007. doi:10.1166/jbn.2013.1594.
42. Mognetti B, Barberis A, Marino S, et al. In vitro enhancement of anticancer activity of paclitaxel by a Cremophor free cyclodextrin-based nanosponge formulation. J Incl Phenom Macrocycl Chem. 2012;74:201-210. doi:10.1007/s10847-011-0101-9.

43. Ferro M, Castiglione F, Punta C, et al. Anomalous diffusion of ibuprofen in cyclodextrin nanosponge hydrogels: An HRMAS NMR study. Beilstein J Org Chem. 2014;10:2715-2723. doi:10.3762/bjoc.10.286.
44. Trotta F, Cavalli R. Characterization and applications of new hyper-cross-linked cyclodextrins. Compos Interfaces. 2009;16(1):39-48. doi:10.1163/156855408X379388.
45. Anandam S, Selvamuthukumar S. Fabrication of cyclodextrin nanosponges for quercetin delivery: Physicochemical characterization, photostability, and antioxidant effects. J Mater Sci. 2014;49:8140-8153. doi:10.1007/s10853-014-8523-6.
46. Darandale SS, Vavia PR. Cyclodextrin-based nanosponges of curcumin: formulation and physicochemical characterization. J Incl Phenom Macrocycl Chem. 2013;75(3-4):315-322. doi:10.1007/s10847-012-0186-9.
47. Ansari KA, Vavia PR, Trotta F, Cavalli R. Cyclodextrin-Based Nanosponges for Delivery of Resveratrol: In vitro Characterisation, Stability, Cytotoxicity and Permeation Study. AAPS PharmSciTech. 2011;12(1):279-286. doi:10.1208/s12249-011-9584-3.
48. Rezaei A, Khavari S, Sami M. Incorporation of thyme essential oil into the β-cyclodextrin nanosponges: Preparation, characterization, and antibacterial activitiy. J Mol Liq. 2021;1241:1-8. https: //doi.org/10.1016/j.molstruc.2021.130610.
49. Mihailiasa M, Caldera F, Li J, Peila R, Ferri A, Trotta F. Preparation of functionalized cotton fabrics by means of melatonin loaded β-cyclodextrin nanosponges. Carbohydr Polym. 2016;142:24-30. doi:10.1016/j.carbpol.2016.01.024.
50. Guntero VA, Peralta M, Noriega P, Kneeteman MN, Ferretti CA. One-Pot Selective Functionalization of Polysaccharides with Urea †. Chem Proc. 2021;3(74):2-6. https://doi.org/10.3390/ecsoc-24-08346.
51. Takeiti CY, Kieckbusch TG, Collares-Queiroz FP. Morphological and Physicochemical Characterization of Commercial Maltodextrins with Different Degrees of Dextrose-Equivalent. Int J Food Prop. 2010;13:411-425. doi:10.1080/10942910802181024.
52. Siemons I, Politiek RGA, Boom RM, van der Sman RGM, Schutyser MAI. Dextrose equivalence of maltodextrins determines particle morphology development during single sessile droplet drying. Food Res Int. 2020;131:1-10. doi:10.1016/j.foodres.2020.108988.
53. Barthold S, Hittinger M, Primavessy D, Zapp A, Groß H, Schneider M. Preparation of maltodextrin nanoparticles and encapsulation of bovine serum albumin – Influence of formulation parameters. Eur J Pharm Biopharm. 2019;142:405-410. doi:10.1016/j.ejpb.2019.07.003.
54. Demasi S, Caser M, Caldera F, et al. Functionalized dextrin-based nanosponges as effective carriers for the herbicide ailanthone. Ind Crop Prod. 2021;164:1-9. doi:10.1016/j.indcrop.2021.113346.