



## A Bibliometric Analysis of Nanocrystalline Cellulose Production Research as Drug Delivery System Using VOSviewer

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### ABSTRACTS

Nanocrystalline cellulose (NCC) has a superiority due to its biocompatibility and biodegradability whose increases the interest of researchers in the field of nanotechnology, especially in drug delivery systems. The purpose of this study is to conduct bibliographical analysis in nanocrystalline cellulose production and its application as a drug delivery system, that combines mapping analysis with VOSviewer software. The reference manager application was used to retrieve survey data. The data obtained is the result of searching for the keyword "nanocrystalline cellulose, drug delivery system". Publish articles related to the topics found as many as 1000 articles between 2017 and 2021. The results showed that nanocrystalline cellulose production research as a drug delivery system increased from 2017 to 2019, but decreased in 2020 to 2021. This study is expected to help researchers carry out and determine targeted research topics and serve as a reference.

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### ARTICLE INFO

**Article History:**

Submitted/Received 09 Dec 2021

First revised 13 Jan 2022

Accepted 15 Jan 2022

First available online 17 Jan 2022

Publication date 01 Sep 2022

**Keyword:**

Bibliometric,  
Drug delivery system,  
Nanocrystalline cellulose,  
Vosviewer.

## 1. INTRODUCTION

Nanocrystalline cellulose is the most abundant natural biopolymer on earth (N. Raghav *et al.*, 2021), isolated from wood (Ditzel *et al.*, 2017), pineapple leaf (Chawalitsakunchai *et al.*, 2021), pineapple peel waste juice (Anwar *et al.*, 2021), olive fiber (Kian *et al.*, 2020), and oil palm empty fruit bunch (Foo *et al.*, 2019). Several methods such as acid hydrolysis, enzymatic hydrolysis, high-intensity ultrasonication, and ball milling are used for nanocrystalline cellulose production (Cui *et al.*, 2016; Qian *et al.*, 2021; Zianor Azrina *et al.*, 2017). Acid hydrolysis is the most commonly used method known in network visualization. It can happen caused acid hydrolysis only takes a short time and the price is relatively cheap, compared to enzymatic hydrolysis. But due to its advantage, acid hydrolysis produced some new toxic compounds that are contaminated in the environment (Karimian *et al.*, 2019).

Nanocrystalline cellulose has proven to be a useful carrier for a variety of drugs routes of administration such as oral, transdermal, and topical. Many reports on nanocrystalline cellulose as a drug delivery system have been undertaken, including research conducted by Neera Raghav and Sharma (2021) on nanocrystalline cellulose-phosphate as an alternative to maintain the continuous release of drugs that cause inflammation by coating with cationic surfactant CTAB (cetyl trimethyl ammonium bromide) and inserting the drug molecules diclofenac, etodolac, ibuprofen and paracetamol (Neera Raghav & Sharma, 2021), Akhvan-Kharazian and Izadi-Vasafi (2019) was modifying the surface of nanocrystalline cellulose with the precursor monomer N-halamine, cyanurate (CYCH), and chlorinated chloropropyl triethoxylan (CPTES) into crosslinking the hydrogel can stop the activity of Staphylococcus and E-coli bacteria (Akhavan-Kharazian & Izadi-Vasafi, 2019). Lugoloobi *et al.* (2021) succeeded in modifying nanocrystalline cellulose with surfactants to form complexes with three cancer drugs that can be released in cancer cells in the bladder by 75% in 2 hours (Lugoloobi *et al.*, 2021).

In recent years, natural polymers-based nanomaterials such as cellulose and its nano-shaped structure, nanocrystalline cellulose (NCC), have a superiority due to their biocompatibility and biodegradability who's increasing the interest of researchers in the field of nanotechnology, especially in drug delivery systems (Neera Raghav & Sharma, 2021). Before conducting research, it is necessary to analyze the topics of interest to be raised as material for discussion in research. This can be done through bibliometric analysis, one way to determine it is by using the VOSviewer. VOSviewer can search for topics that offer research opportunities and find the most commonly used references in a particular field (Nandiyanto *et al.*, 2020).

In this study, the trend of research was analyzed regarding nanocrystalline cellulose production research as a drug delivery system over the last five years from 2017 to 2021. This study aims to conduct bibliometric analysis research in nanocrystalline cellulose as a drug delivery system. Bibliometric analysis was carried out on the VOSviewer application with a database derived from google scholar and integrated into the publish or perish application. This study is intended to assist and help researchers in conducting and deciding on research topics. Specially to complete in the field of nanocrystalline cellulose production and its application as a drug delivery system researcher as a consideration for determining the research theme to be taken.

## 2. METHODS

Data analysis in this research was obtained from published and indexed articles by Google Scholar which is collected from 1000 articles in the range of 2017-2021, including original

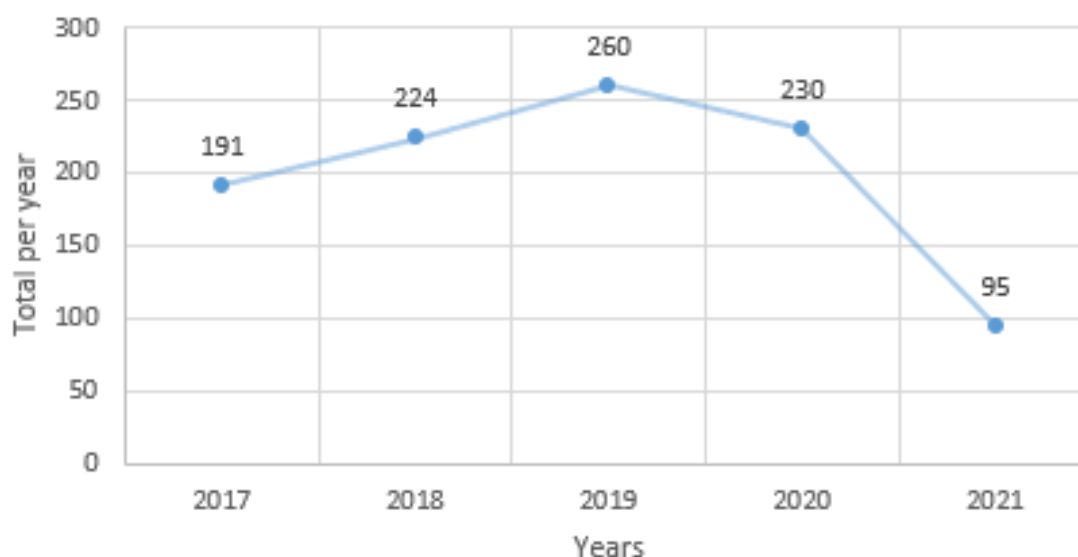
research, articles, and review articles. All of the articles were written in English. Publish or perish as reference manager application was used to obtain the research data. 1000 data was related to the topic production and application of nanocrystalline cellulose as a drug delivery system. Those publications were retrieved in RIS format to be analyzed in VOSviewer.

VOSviewer was chosen to visualize and analyze trends in the form of bibliometric maps. The data mapping articles from publish or perish database have been prepared and presented in VOSviewer by network visualization, density visualization, and overly visualization. Those visualizations were presented in this study.

### 3. RESULTS AND DISCUSSION

#### 3.1. Research Developments in The Field of Fe<sub>3</sub>O<sub>4</sub> Nanoparticle Production

The research database from Publish or Perish was sorted by year of research. Figure 1 shows a curve from a level of development of the research of nanocrystalline cellulose for drug delivery systems over the last five years, in a range from 2017 to 2021. The level of research on nanocrystalline cellulose continued to increase constantly from 2017 as many as 191 papers, in 2018 around 224 papers, until 2019 it reached 260 papers. However, the research related to this topic has decreased since 2020 to 230 and continues to decline in 2021 until it reaches 95 papers.



**Figure 1.** Level of development of research on nanocrystalline cellulose production as drug delivery system.

#### 3.2. Visualization Fe<sub>3</sub>O<sub>4</sub> Nanoparticle Production Topic Area Using VOSviewer

The related research to nanocrystalline cellulose for drug delivery systems is divided into 7 clusters, namely:

- (i) Cluster 1 has 37 items, the 37 items are acid hydrolysis, amorphous region, biomedical field, biomedicine, biosensor, category, cellulose material, cellulose nanowhisker, cellulose whisker, cellulosic material, cnfs, cnw, cnws, cotton, critical review, implant, isolation, MCC, microcrystalline cellulose, microfibrillated cellulose, nanofibril, nanofibrillated cellulose, nanowhisker, native cellulose, needle, nfc, preparation method, rod, sensor, source spherical cellulose nanocrystal, state, sulfuric acid hydrolysis, wastewater treatment, water purification, whisker, and wood.

- (ii) Cluster 2 has 37 items, the 37 items are alginate, anticancer drug, cancer therapy, carboxymethyl cellulose, carrier system, cellulose acetate, chemotherapy, concentration, construction, coworker, current status, doxorubicin, drug administration, effective drug delivery system, electrospun nanofiber, ethylcellulose, fda, folic acid, graphene, inorganic nanocrystal, lignin, limitation, liposome, loading, methotrexate, mixture, nanocarrier, opportunity, oral drug delivery, polysaccharide, problem, quantum dot, release behavior, smart drug delivery system, us food, and tumor.
- (iii) Cluster 3 has 36 items, the 36 items are biodegradable polymer, conventional drug delivery system, DDS, drug delivery carrier, drug delivery device, drug molecule, filler, influence, injection, kind, lactic acid, low cost, microneedle, nano cellulose, nanocellulose particle, nanocomposite film, oral administration, polymer matrix, polyvinyl alcohol, potential application, potential drug delivery system, potential use, pva, reinforcement, release rate, rheology, rice huck, sodium alginate, suspension, sustained release, transdermal drug delivery system, transdermal drug delivery, utilization, vinyl alcohol, vitro, and vitro evaluation.
- (iv) Cluster 4 has 31 items, the 31 items are acrylic acid, amount, analysis, biodegradability, cancer treatment, CMC, colon, dox, drug loading, drug release behavior, drug release kinetics, drug release profile, graphene oxide, impact, ion, microsphere, model drug, n-isopropyl acrylamide, nanocomposite hydrogel, natural polysaccharide, new drug delivery system, order, presence, regenerative medicine, release profile, release system, removal, sodium, tempo, and vitro release.
- (v) Cluster 5 has 25 items, the 25 items are administration, bacterial, bacterial nanocellulose, bnc, chitosan nanoparticle, collagen, combination, comprehensive review, dressing, drug nanocrystal, hpmc, literature, medical device, nanosuspension, ncs, novel, number, recent progress, regard, section, silver nanoparticle, stabilizer, tissue engineering application, wound, and topical drug delivery.
- (vi) Cluster 6 has 23 items, the 23 items are bacterial cellulose nanocrystal, bioavailability, cellulose nanomaterial, efficiency, emulsion, encapsulation, future prospect, hydrophobic drug, hydrophobic drug delivery, nano, nanomedicine, nanotechnology, oil, pharmaceutical science, the present study, prospect, recent development, reduction, self, soluble drug, therapeutic agent, transdermal delivery, and water-soluble drug.
- (vii) Cluster 7 has 22 items, the 22 items are biomedical engineering, cellular uptake, chapter, chemical, comparison, efficient drug delivery system, engineering, extraction, hydrolysis, ionic liquid, medical application, medical implant, nanocellulose material, nanocrystalline, pharmaceutical, plant, processing, promising material, tissue, topical drug delivery system, toxicity, and wide range.

Cluster 1 is marked by purple color, cluster 2 is marked by orange color, cluster 3 is marked by blue sky color, cluster 4 is marked by green color, cluster 5 is marked by red color, cluster 6 is marked by red color, and cluster 7 is marked by dark green color.

### **3.3. Research Developments in The Field of Fe<sub>3</sub>O<sub>4</sub> Nanoparticle Production**

The research database from Publish or Perish was sorted by keyword and title of research. Figure 2 shows the relationship between terms in the topic of nanocrystalline cellulose for drug delivery systems whose terms are connected by networks or lines. Figure 2 shows the clusters of each of the investigated fields of research, such as nanocrystalline cellulose or cellulose nano whiskers in cluster 6 with a total link strength of 74 and occurrence of 27. Nanocrystalline cellulose was connected to the term biomedical field in cluster 3, drug delivery in cluster 4, topical and transdermal drug delivery system in cluster 5.



- Anwar, B., Bundjali, B., Sunarya, Y., and Arcana, I. M. (2021). Properties of bacterial cellulose and its nanocrystalline obtained from pineapple peel waste juice. *Fibers and Polymers*, 22(5), 1228–1236.
- Chawalitsakunchai, W., Dittanet, P., Loykulnant, S., Sae-oui, P., Tanpichai, S., Seubsai, A., and Prapainainar, P. (2021). Properties of natural rubber reinforced with nano cellulose from pineapple leaf agricultural waste. *Materials Today Communications*, 28, 102594.
- Cui, S., Zhang, S., Ge, S., Xiong, L., and Sun, Q. (2016). Green preparation and characterization of size-controlled nanocrystalline cellulose via ultrasonic-assisted enzymatic hydrolysis. *Industrial Crops and Products*, 83, 346–352.
- Ditzel, F. I., Prestes, E., Carvalho, B. M., Demiate, I. M., and Pinheiro, L. A. (2017). Nanocrystalline cellulose extracted from pine wood and corncob. *Carbohydrate Polymers*, 157, 1577–1585.
- Foo, M. L., Tan, C. R., Lim, P. D., Ooi, C. W., Tan, K. W., and Chew, I. M. L. (2019). Surface-modified nanocrystalline cellulose from oil palm empty fruit bunch for effective binding of curcumin. *International Journal of Biological Macromolecules*, 138, 1064–1071.
- Karimian, A., Parsian, H., Majidinia, M., Rahimi, M., Mir, S. M., Samadi Kafil, H., Shafiei-Irannejad, V., Kheyrollah, M., Ostadi, H., and Yousefi, B. (2019). Nanocrystalline cellulose: Preparation, physicochemical properties, and applications in drug delivery systems. *International Journal of Biological Macromolecules*, 133, 850–859.
- Kian, L. K., Saba, N., Jawaid, M., Alothman, O. Y., and Fouad, H. (2020). Properties and characteristics of nanocrystalline cellulose isolated from olive fiber. *Carbohydrate Polymers*, 241, 116423.
- Lugoloobi, I., Maniriho, H., Jia, L., Namulinda, T., Shi, X., and Zhao, Y. (2021). Cellulose nanocrystals in cancer diagnostics and treatment. *Journal of Controlled Release*, 336, 207–232.
- Nandiyanto, A. B. D., Biddinika, M. K., and Triawan, F. (2020). How bibliographic dataset portrays decreasing number of scientific publications from Indonesia. *Indonesian Journal of Science and Technology*, 5(1), 154–175.
- Qian, M., Lei, H., Villota, E., Zhao, Y., Wang, C., Huo, E., Zhang, Q., Mateo, W., and Lin, X. (2021). High yield production of nanocrystalline cellulose by microwave-assisted dilute-acid pretreatment combined with enzymatic hydrolysis. *Chemical Engineering and Processing - Process Intensification*, 160, 108292.
- Raghav, N., Sharma, M. R., and Kennedy, J. F. (2021). Nanocellulose: A mini-review on types and use in drug delivery systems. *Carbohydrate Polymer Technologies and Applications*, 2, 100031.
- Raghav, N., and Sharma, M. R. (2021). Usage of nanocrystalline cellulose phosphate as novel sustained release system for anti-inflammatory drugs. *Journal of Molecular Structure*, 1233, 130108.
- Zianor Azrina, Z. A., Beg, M. D. H., Rosli, M. Y., Ramli, R., Junadi, N., and Alam, A. K. M. M. (2017). Spherical nanocrystalline cellulose (NCC) from oil palm empty fruit bunch pulp via ultrasound assisted hydrolysis. *Carbohydrate Polymers*, 162, 115–120.