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Characterization of nano encapsulated cinnamon bark extract (*Cinnamomum burmannii*) based on chitosan alginate as a potential drug delivery system for cervical cancer therapy

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Abstract

Objective: This study aims to evaluate the nanoencapsulation potential of cinnamon extract based on the results of characterization tests.

Method: Formulation F2 using a combination of 1% chitosan and 1.5% alginate showed optimal characterization results compared to F1 and F3.

Results: The results showed that formulation F2 had a particle size of 246.3 nm, PDI of 0.396, and zeta potential of -33.8 mV indicating good physical stability, homogeneous particle distribution, and suitable particle size for nanoencapsulation applications. In addition, particle visualization showed clear and uniform physical properties, while a pH test of 7.32 supported suitability for oral delivery.

Conclusion: Based on these characterization results, nanoencapsulation of cinnamon bark extract using chitosan alginate polymer shows significant potential as a drug delivery system for cervical cancer therapy

Keywords: Alginate; Cervical Cancer; Chitosan; *Cinnamomum burmannii*; Nanoencapsulation

1. Introduction

Cervical cancer is a global health problem that has increased rapidly over the past few decades. According to the World Health Organization (WHO) in 2020, there were 604,000 new cases with a total of 342,000 deaths occurring due to cervical cancer [1]. In Indonesia, the incidence of cervical cancer is very high. In 2021, cervical cancer cases increased by 36,633 cases or 17.2% of all cancer cases in women with the highest number of cases found in East Java Province. Until now, cervical cancer is still ranked in the top three as the cancer with the largest number of deaths in Indonesia [2]. Research mentioned that most cervical cancer treatments are carried out by administering chemotherapeutic agents doxorubicin, carboplatin, celecoxib, and paclitaxel with high systemic toxicity and are not selective, causing damage to normal tissues [3].

The potential of cinnamon bark extract as an anticancer agent has been proven in several studies. Cinnamon ethanol extract has a very strong antioxidant with an IC50 value of 6.28 µg/mL [4]. According to research by Jaisamak et al. [5] The cinnamaldehyde compound in cinnamon ethanol extract was shown to have anticancer effects on C-33A cancer cell

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lines in vitro. Bioactive compounds contained in cinnamon extracts are considered potential as anticancer agents, but low bioavailability and chemical stability as well as large particle sizes are constraints to their biomedical applications.

Nanoencapsulation is a method that can provide protection for bioactive compounds that are easily degraded. The very small size of nanocapsules can increase the bioavailability of compounds [6]. Nanoencapsulation with chitosan is widely researched in drug delivery systems due to several advantages, one of which is increasing target specificity. Chitosan is a U.S. Food and Drug Administration (FDA)-approved biopolymer with excellent biological properties, including antitumor, antioxidant, antimicrobial, and wound-healing activities, making it suitable for biomedical applications, the insolubility of chitosan at physiological pH can be overcome by chemical modification of amino groups resulting in soluble derivatives and expanding applications [7]. Sorasitthiyanukarn et al. [8] modified drug delivery with chitosan and alginate which was shown to improve mucoadhesive properties for oral drug application.

Based on the above problems, it is necessary to conduct a characterization study of the results of cinnamon extract nanoencapsulation synthesis including FTIR, visualization, pH, polydispersity index (PDI), Particle Size Analyzer (PSA), Zeta Potential, and Scanning Electrone Microscope to determine its potential as a candidate drug delivery system in cervical anticancer therapy.

2. Material and methods

This research is a type of laboratory experimental research to determine the potential of nanoencapsulation of cinnamon extract (*Cinnamomum burmannii*) based on chitosan alginate as a candidate drug delivery system in cervical anticancer therapy based on the results of characterization tests. The research was done experimentally for 4 months (April 19 - August 18, 2024).

2.1. Plant Identification

Plant identification was performed to ensure that the cinnamon used was cinnamon with the species name *Cinnamomum burmannii* [9].

2.2. Extraction of Cinnamon Bark

Fresh cinnamon bark is then sorted, washed with flowing water until clean, drained, then aired without exposure to direct sunlight. The symplisia was then pulverized with a grinding tool. The method used for extraction is the maceration method by soaking 500 grams of cinnamon powder in 96% ethanol which is allowed to stand for 24 hours.

2.3. Preparation of Cinnamon Extract Nanoencapsulated

The nanoencapsulated preparation formula is varied with a combination of two different polymer solutions, namely chitosan and alginate, which play an important role in encapsulating cinnamon extract in an optimal nanoencapsulated form so as to increase the bioavailability of cinnamon extract [10]

Table 1 Cinnamon extract nanoencapsulation formulation

Ingredients	**Function**	**F1**	**F2**	**F3**
Cinnamon Extract 5%	Active Ingredients. Oil Phase	0,8 mL	0,8 mL	0,8 mL
Chitosan	Water Phase	5 mL (1%)	5 mL (1%)	5 mL (1,5%)
Alginate	Water Phase	11 mL (1%)	11 mL (1,5%)	11 mL (1%)
Tween 80 3%	Surfactan	3,4 mL	3,4 mL	3,4 mL
STPP	*Crosslinker*	10 mL	10 mL	10 mL
Total	-	21 mL	21 mL	21 mL

The nanoencapsulation preparation stage was carried out by making 5% cinnamon extract. In another glass beaker, the aqueous phase was prepared in the form of chitosan and alginate according to the formula, namely F1, F2, and F3 according to the ratio. The chitosan alginate solution was stirred at a constant speed of 1500 rpm for 2 hours until homogeneous, then 1 ml of 1% w/v STPP solution was added. The oil phase was prepared by adding 3% tween as much

as 3.4 ml into the cinnamon extract solution and stirred until homogeneous for 10 minutes at 1500 rpm. Next, the oil phase was mixed into the water phase at 1500 rpm for 2 hours. Next, the oil phase was mixed into the water phase at 1500 rpm for 2 hours. The mixture of the two phases was nanoencapsulated using an ultrasonic bath for 10 minutes at a frequency of 70 kHz followed by an ultrasonic probe at 40 khZ for 2 minutes without pause.

2.4. Characterization

2.4.1. Visualization Test

Visualization test by observing the physical appearance of the nanoencapsulated preparation which includes shape, color, clarity, and phase separation of the preparation using the five senses [11].

2.4.2. pH Test

The pH meter was calibrated with a pH 7.00 aqueous solution before pH measurement. The targeted nanoencapsulated met the pH specification of a good oral application of about 5 – 7.5 [12].

2.4.3. Particle Size and Homogenity Test

Size and size distribution measurements were carried out using a Particle Size Analyzer. Nanoencapsulated samples were shaken to homogenize the liquid and then observed at an angle of 165º with a temperature of 25ºC. Data observed were average droplet diameter and polydispersity index (PDI).

2.4.4. Zeta Potential

The optimum zeta potential value of the nanoencapsulation formula ranges from more than +30 mV or less than -30 mV [13].

2.4.5. Efficiency Test of Nanoencapsulation by UV-Vis

The absorption efficiency test was by centrifuging the nanoencapsulated results at 1200 rpm for 30 minutes then the supernatant was taken to be analyzed using a Uv-Vi's spectrophotometer [10].

2.4.6. FTIR Test

Functional group test with FTIR (Fourier Transform Infrared) spectroscopy to determine the functional group of the compound. The results are obtained by comparing between the absorption lines produced [14].

2.4.7. Morphology Test of Nanoencapsulation With SEM

The surface morphology of the nanoencapsulation was characterized by Scanning Electron Microscope (SEM). Samples were dried using a freeze dryer and then measured at magnifications ranging from 1000x, the successfully formed nanoencapsulation will show a spherical nanocapsule morphology [15].

2.5. Data Analysis

Data analysis regarding the characterization and visualization of cinnamon (*Cinnamomum burmannii*) extract nanoencapsulation was carried out descriptively by comparing the results obtained with the results found in journal articles and previous research.

3. Results and Discussion

This section will explain the results of the first process of determining cinnamon to formulating chitosan alginate-based nanoencapsulated formulations as an anticancer of the cervix to characterization testing. The results of the plant determination test used are cinnamon with the species name *Cinnamomum burmannii* from the Lauraceae tribe. The resulting cinnamon extraction results showed a yield percentage of 24.26%b/b. The visualization test aims to check the visual appearance of cinnamon extract nanoencapsulation preparation. Good nanoencapsulation is characterized by clarity and translucency [16]. Based on the visualization test, F1 and F2 preparations met the requirements of a good visualization test.

Table 2 Visualization test results Nanoencapsulation of Cinnamon Extract

Test	F1	F2	F3
Visualization	Orange, clear, cinnamon aroma	Orange, clear, cinnamon aroma	Orange, cloudly cinnamon aroma

Figure 1 Physical appearance of cinnamon extract nanoencapsulation

pH testing using a pH meter that has been calibrated with a pH 7.00 dapar solution shows that the results of the nanoencapsulation pH test meet the pH standards of good oral preparations, namely 5-7.5 [12].

Table 3 Results of pH Testing Nanoencapsulation of Cinnamon Extract

Test	F1	F2	F3
pH	7.07±0.008	7.32±0.005	7.19±0.009

FTIR testing was performed to confirm the bonds formed in all nanoencapsulated formulations, both with and without extracts and each was compared with the ingredients used before formulation

Table 4 FTIR Analysis of Functional Groups

Bond	Chitosan (CHI)	Alginat (AG)	Ekstract (CE)	F1 CHI-AG-CE	F2 CHI-AG-CE	F3 CHI-AG-CE	F1 CHI-AG	F2 CHI-AG	F3 CHI-AG
NH strech	3481	-	3349	3403	3425	3419	3604	3421	3417
C=O	-	-	1661	1732	1714	1717	-	-	-
COO- strech	-	1583	-	1582	1581	1591	1594	1589	1585
N-H bending	1587	-	-	1582	1581	1591	1594	1589	1585
C=C strech	-	-	1447	1435	1435	1436	-	-	-
COO- strech	-	1383	-	1404	1405	1405	1406	1405	1405

The graph on F1-F3 CHI-AG-CE shows the absorption of a shift in the characteristic peak of chitosan, namely the N-H group from 348 cm-1 and amide II N-H bond which shifts from 1587 cm-1, shifting the characteristic peak of alginate in the 1583 cm-1 region for asymmetric -COO bonds and 1383 for symmetrical -COO bonds as carboxylate groups. The shift that occurs indicates a polyelectrolyte complexation reaction between chitosan and alginate [17], The characteristic peak of the extract is the absorption in the 1661 cm-1 region indicating the presence of a C=O carbonyl group, and in the 1447 cm-1 region for the C=C group [18].

Furthermore, nanoencapsulated preparations that meet the requirements of oral preparations have a size of less than 300 nm. The polydispersity index (PDI) indicates uniform size if the PDI value is <0.5 [13].

Table 5 Particle Size and Homogeneity Test Results

Formula	PDI	Size
F1	0.662	390.0 nm
F2	0.396	246.3 nm
F3	0.135	602.0 nm

Table 5 shows that F2 and F3 meet the requirements for a good PDI size, while the nanoencapsulation size test results show that only F2 meets the nanoencapsulation size for peroral preparation. Furthermore, the three formulas were tested for stability using the zeta potential method. The optimal zeta potential value of nanoencapsulated preparations is more negative than -30mV, indicating that the preparation is stable [13].

Table 6 Stability Test Result of Nanoencapsulation

Test	F1	F2	F3
Stability	-36.1 mV	-33.8 mV	-31.7 mV

All three formulations met a good zeta potential value because it was more negative than -30 mV. Furthermore, the efficiency of cinnamon extraction nanoencapsulation was tested by UV-Vis Spectrophotometry.UV-Vis.

Table 7 Results of Nanoencapsulation Efficiency Tets

Test	F1	F2	F3
Efficiency	83.52%	89.36%	83.52%

Table 7 shows that F2 has the highest percentage level for nanoencapsulation efficiency. The absorption efficiency test was conducted to determine the percentage of extract that was successfully absorbed in the nanocapsules [10]. Based on the results of the characterization test, F2 is the most optimal formulation in accordance with the oral preparation requirements. Furthermore, F2 was used to confirm the morphology. The round morphological shape indicates that the nanoencapsulation is formed [15].

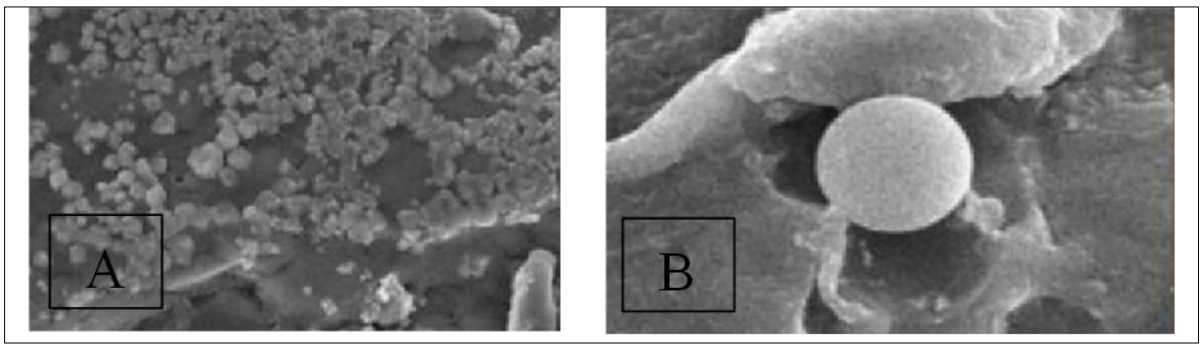

Figure 2 Morphological Results of Nanoencapsulation by *Scanning Electron Microscope* (A) magnification 5000x (B) magnification 7500X

4. Conclusion

Based on this study, it was concluded that nanoencapsulation of cinnamon extract (*Cinnamomum burmannii*) based on chitosan alginate has the potential to be used as a candidate drug delivery system for cervical anticancer therapy, with formulation F2 as the selected formula. Formulation F2 has optimal characterization test results, namely clear visual appearance, pH 7.32 ± 0.005 which is suitable for oral preparations, particle size 246.3 nm with PDI 0.396 which indicates homogeneous particle distribution, zeta potential - 33.8 mV which is stable, and zeta potential - 33.8 mV which

is stable, the highest encapsulation efficiency of 89.36% and has morphological characteristics that are suitable for further development.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] World Health Organization. HPV and Cervical Cancer. 2023. URL: https://www.who.int/news-room/factsheets/detail/cervicalcancer?gad_source=1&gclid=

[2] Minanton M, Rosa S, Oktavia LRD, and Rahagia R. Analysis of Factors Related to Early Detection Behavior of Cervical Cancer in KB Acceptors. Citra Delima Scientific journal of Citra Internasional Institute. 2024; 7(2): 105-111. doi: 10.33862/citradelima.v7i2.385

[3] Robledo-Cadena DX, Gallardo-Pérez JC, Dávila-Borja V, Pacheco VSC, Belmont-Díaz JA, Ralph SJ, Blanco-Carpintero BA, Moreno-Sánchez R and Rodríguez-Enríquez S. Non-Steroidal Antiinflammatory Drugs Increase Cisplatin, Paclitaxel, and Doxorubicin Efficacy Against Human Cervix Cancer Cells. Pharmaceuticals. 2020; 13 (12):463. doi: 10.3390/ph13120463

[4] Tampubolon AR. Formulation and Effectiveness Test of Anti-Aging Peel-Off Gel Mask Preparation Containing Ethanol Extract of Cinnamon Bark (Cinnamomum burmannii (C. Ness & T. Ness) C. Ness ex Blume). [Dissertation]. Universitas Sumatera Utara. 2021.

[5] Jaisamak K, Iawsipo P, and Ponglikitmongkol M. Anti-Invasion activity of Trans-4-Methoxy-Cinnamaldehyde (4-MCA) in Cervical Cancer Cells. Proceedings of the 6th International Conference on Biochemistry and Molecular Biology (BMB 2018), 20-22 Juni 2018, Tokyo, Japan. pp. 18-20.

[6] Salah M, Mansour M, Zogona D, and Xu X. Nanoencapsulation of anthocyanins-loaded β-lactoglobulin nanoparticles: Characterization, stability, and bioavailability in vitro. Food Research International. 2020. 137. 109635. doi: 10.1016/j.foodres.2020.109635

[7] Niculescu AG, and Grumezescu AM. Applications of chitosan alginate based nanoparticles—An up-to-date review. Nanomaterials. 2022; 12(2): 186. doi: 10.3390/nano12020186

[8] Sorasitthiyanukarn FN, Muangnoi C, Bhuket PRN, Rojsitthisak P, and Rojsitthisak P. Chitosan/Alginate Nanoparticles as A Promising Approach for Oral Delivery of Curcumin Diglutaric Acid for Cancer Treatment. Materials Science and Engineering: C. 2018; 93: 178-190. doi: 10.1016/j.msec.2018.07.069

[9] Astika RY. Anti-inflammatory Activity Test of Ethanol Extract of Cinnamon Leaves (Cinnamomum burmannii) in Male White Mice. Jurnal Ilmiah Manuntung. 2022; 8(1): 14-23.

[10] Hatmayana R, Noval N, Mahdiyah D, Ramadhani RA, and Auliyani N. Characterization of Serunai Leaf Extract Nanocapsules (Chromolaena odorata L.) with Chitosan-Alginate Variations Using Emulsion-Diffusion Method. Jurnal Surya Medika (JSM). 2022; 8(3): 187-194. doi: 10.33084/jsm.v8i3.4512

[11] Ovilia O, Hutahaen TA, and Februyani N. Black Glutinous Rice Body Scrub Formulation (Oryzae Sativa L. var glutinous) as a Natural Skin Moisturizer. Indonesian Journal of Health Science. 2023; 3(2a): 396-402. doi: 10.54957/ijhs.v3i2a.510

[12] Husni P, Hisprastin Y, and Januarti M. Formulation and Physical Stability Test of Sardinella lemuru Fish Oil Emulsion Preparation. As-Syifaa Jurnal Farmasi. 2019; 11(02): 137-146.

[13] Banerjee A, Qi, J, Gogoi R, Wong J, and Mitragotri S. Role of nanoparticle size, shape and surface chemistry in oral drug delivery. Journal of Controlled Release. 2016; 238: 176-185. doi: 10.1016/j.jconrel.2016.07.051

[14] Soussi S, Essid R, Karkouch I, Saad H, Bachkouel S, Aouani E, and Tabbene O. Effect of lipopeptide-loaded chitosan nanoparticles on Candida albicans adhesion and on the growth of Leishmania major. Applied Biochemistry and Biotechnology. 2021; 193(11): 3732-3752. doi: 10.1007/s12010-021-03621-w

[15] Ahmad RM, Greish YE, El-Maghraby HF, Lubbad L, Makableh Y, and Hammad FT. Preparation and characterization of blank and nerolidolloaded chitosan–alginate nanoparticles. Nanomaterials. 2022; 12(7): 1183. doi: 10.3390/nano12071183

[16] Sadeq ZA. Review on Nanoemulsion: Preparation and Evaluation. International Journal of Drug Delivery Technology. 2020; 10(1): 187189. doi: 10.25258/ijddt.10.1.33

[17] Riyandari BA, Rizki YT, and Ramdani M. Synthesis of Polyelectrolyte Complex Films of Chitosan-Alginate by Addition of Kelor Leaves Extract (Moringa oleifera) for Food Packaging. Jurnal Kimia Riset. 2022; 7(2). doi: 10.20473/jkr.v7i2.28954

[18] Alvear GA, Pineda-Aguilar N, Lozano P, Lárez-Velázquez C, Suppan G, Galeas S, and López F. Synergistic Antibacterial Properties of Silver Nanoparticles and Its Reducing Agent from Cinnamon Bark Extract. Bioengineering. 2024; 11(5): 517. doi: 10.3390/bioengineering11050517.