Study of Core Shell n-Octyl Cinnamate in Nano Particle as Anti-Inflamatories

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Study of Core Shell n-Octyl Cinnamate in Nano Particle as Anti-Inflamatories

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Abstract:N-octyl cinnamic is a compound that has potential as a drug as an antioxidant, anti-inflammatory, but is constrained by the nature of n-octyl cinnamate which is difficult to dissolve in water, causing low bioavailability in the systemic circulation. To overcome this problem, curcumin is formulated in the form of nanoparticles using chitosan polymer, a derivative of chitin which can be obtained from crab and shrimp shell waste. This study aims to synthesize n-octyl cinnamic nanoparticles using a simple coating method using chitosan and sodium alginate and to evaluate the stability of the nanoparticles in vitro. The characterization of nanoparticles that was carried out included adsorption efficiency tests, particle size determination using a Particle Size Analyzer and morphological observations using a Transmission Electron Microscopy (TEM) tool. The anti-inflammatory activity test was carried out to determine the potential of the synthesized compound using the Bovine Serum Albumin (BSA) method. The results showed that the nanoparticle formula contained n-octyl cinnamic composition with an adsorption % of 91.02%. The particle size is 68.1 nm based on particle size analyzer testing with an average size of 519.6 . The morphological observations showed that the particles were spherical in shape with an uneven surface. The n-octyl cyanamate/Alginate/Chitosan nanoparticles have anti-inflammatory activity with a % protein denaturation inhibition of 97.71%. This indicates that n-octyl cyanamate/Alginate/chitosan nanoparticles have the potential to be developed as an anti-inflammatory drug delivery system.
Keywords: Nanoparticle, Anti-inflammatory, n-octyl cyanamate/Alginate/chitosan, Synthesis.

I. INTRODUCTOION

Cinnamic acid and its derivatives from the shikimic acid biosynthetic pathway are prominent. Since the dawn of civilization, they have been used in traditional medicine due to their several therapeutic actions, such as antiseptic, insecticidal, stimulant, and carminative.[1],[2]. Taking into account the interaction between the structure and the target molecule, cinnamic acid and its derivatives continuously have several biological activities. However, the concentrations found in plant sources are low, and their use on a large scale is not feasible. On the other hand, with organic synthesis, it is possible to obtain a large number of molecules from simple to complex structures and contribute to the industrial market[3]. Based on this, the study of medicinal chemistry applying organic synthesis and computational methods may largely contribute to the development of new drugs. In addition, the compound presents a simple structure, which allows large-scale production[4].

One of the cinnamic derivatives that can be synthesized is n-octyl cinnamate. This compound can be synthesized through an esterification reaction between cinnamic acid and octanol with concentrated sulfuric acid as catalyst. Esterification is a simple method for converting organic acids, in this case carboxylic acids, into their ester derivatives. Esterification with the help of an acid catalyst is common in making esters[5]. This compound is a derivative of cinnamic acid in its ester form with n-octanol saturated alcohol.

n-octyl cinnamic was successfully synthesized by pearls in 2021 using ultrasonic waves and seeing its great activity as an antioxidant and anti-inflammatory. Seeing its enormous potential, to increase its potential application in clinical terms, several formulation strategies have been developed, one of which is formulation in the field of nanotechnology.[6]. Nanotechnology has provided many benefits in the pharmaceutical, cosmetic, etc[7]. The use of cinnamic acid as an antibacterial is still limited due to its low solubility in water. Therefore, efforts are needed to overcome the shortage of cinnamic acid, one of which is nanotechnology. The application

of nanotechnology can improve its thermal stability, oral bioavailability, and water solubility (Huang dkk., 2010).

One of the nanotechnology in the formulation is the core shell. Core shell nanoparticles are heterogeneous NPs consisting of two or more materials (metals, elements, or biomolecules) one nanomaterial acting as a central core while the other materials/materials are located around a central core (shell) [8]. Core shells have been actively dominating in nanoparticle formulations and offer great benefits especially in drug delivery systems[7], [9]The surface layer covering the core can lead to decreased toxicity and increased biocompatibility there in[9]·[10]. Soppimath et al., have succeeded in synthesizing a core shell that is responsive to pH and drug molecule delivery[9]. Within a lipid core shell stabilized by Pluronic F-127 polymer, the lipids of the core shell are highly effective in controlling the release of proteins such as vascular endothelial growth factor as well as the core shell presenting opportunities for surface modification for targeted delivery[9].

Based on the background above, this study formulated core-shell nanoparticles using polymers, one of which is chitosan. Chitosan is a natural biopolymer and is easily obtained from the deacetylation process of chitin compounds in the shells of crustacean animals such as crabs and shrimp. Chitosan is non-toxic, biodegradable, biocompatible and mucoadhesive The technique used in this study was chitosan-coated n-octyl cinnamic so that it was easy to reach the desired target and the addition of chitosan prevented degradation and increased biostability.[11].

II. MATERIALS AND METHODS

2.1 Chemicals

The materials used in this study were benzaldehyde, malonic acid, β-alanine, pyridine, ethanol p.a (Merck), anhydrous MgSO4, glacial acetic acid, chitosan, sodium alginate, ethanol, CaCl2, ethyl acetate, concentrated sulfuric acid, acetone. , Octanol (Merck), silica gel GF 254 distilled water. chloroform, acetone, aquabides, acetic acid anhydride, BSA.

2.3 Instrumentation

The tools used in this study were glassware in the laboratory, sonicator, IR spectrometer, H-NMR spectrophotometer, melting point apparatus, GC-MS, Particle Size Analyzer (PSA). , Transmission Electron Mycroscopy (TEM), Vacuum rotary evaporator, Buchner filter, TLC plate, UV-Vis spectrophotomer, G60F254 silica gel plate, melting point apparatus and capillary tube.

2.4 Synthesis of n-Octyl Cinnamic

Synthesis of n-octyl cinnamic using a procedure based on Nurul Hijjati et al (2008) with slight modifications[12]. Into the Erlenmeyer put ± 0.246 mol of cinnamic acid and 2.5 mol of n-octanol and 2.7 ml of concentrated H_2SO_4, and boiling stones. The mixture was sonicated at 70^0C and 7 hours sonication time.Then the residue was poured into a separatory funnel and anhydrous $NaHCO_3$ solution was added until the atmosphere was neutral. Then after the pH was neutral, ether was added. Then the ether phase was separated and anhydrous $MgSO_4$ was added in a separatory funnel and then shaken for 5 minutes and left for 20 minutes. The two were separated by filtering and then evaporated to remove the remaining n-octanol. The residue is extracted with hexane. The extract obtained was purified by column chromatography. The stationary phase used was silica gel G60 F254 and n-hexane: ethyl acetate: acetone (65: 15: 5) as eluent. Then the filtrate was cooled to obtain n-octyl cinnamic crystals. The synthesized compound was tested for melting point using melting point apparatus, IR.

2.5 Alginate/chitosan/n-octyl cinnamate core shell synthesis

The synthesis of core shell nanoparticles of Alginate/Chitosan/n-octyl cinnamate was carried out by a gradual mechanism of forming the core shell. The first stage was carried out using a gelation technique by making a 0.3% solution of n-octyl cinnamic in 70% ethanol which was mixed dropwise into a 0.2% chitosan solution in 0.1 M acetic acid pH 5. The ratio of the solutions made was 1: 10 and 10:1 [13]. The solution was stirring for 30 minutes. The second stage was the addition of a mixture of 20 mL of 0.2% Sodium Alginate solution and 10 mL of 0.3% $CaCl_2$. The solution was continued stirring for 30 minutes and continued stirring for 1 hour. The resulting precipitate was centrifuged at 5000rpm for 20 minutes. The solution was washed with 0.05% NaCl 2 times[14]. The resulting nanoparticles were stored in demineralized aquadest.

2.6 TEM Test and Particle Size Distribution

The particle size distribution was carried out by measuring the diameter of the nanoparticles in the suspended liquid. Two drops of the nanoparticle sample were put into the cuvette and 5 mL of distilled water was added. Particles were measured with (Zetasizer ZS nano). The wavelengths used were used and all measurements were made in triplicate and sizes are expressed in nm ± SD. The particle size distribution is expressed in the form of a

polydispersity index (PDI). The morphology of the nanoparticles was tested using TEM tools

2.7 Nanoparticle Adsorption Efficiency Test

Adsorption efficiency of n-Octyl cinnamic in chitosan/alginate complex was carried out using the extraction method. A total of 3 x 7.5 mL of the nanoparticle formula was precipitated by centrifugation at 6,000 rpm for 45 minutes and then added ethyl acetate to a volume of 14 mL. Free N-octyl cinnamic (not adsorbed in the chitosan/alginate complex) in the supernatant was extracted by mixing using a vortex mixer for 1 minute. The absorbance of the ethyl acetate phase was measured using a spectrophotometer at the maximum wavelength of n-octyl cinnamate to determine the free n-octyl cinnamate[15].

2.8 In Vitro Anti-Inflammatory Test

In vitro anti-inflammatory test was carried out based on the research method by (Williams et al., 2008)[16]. Stages of testing the activity of the synthesis results against denaturation of Bovine Serum Albumin (BSA). A total of 5 ml of the positive control solution consisted of 4,950 μl of BSA and 50 μl of diclofenac sodium solution. Control solutions were made in various concentrations, namely 1000 ppm, 100 ppm, 10 ppm, and 1 ppm. Each solution was vortexed, then incubated for 30 minutes at room temperature (27ºC). After that it was heated for 25 minutes at 90ºC. Then left at room temperature (27ºC) for 25 minutes. Then the turbidity was measured with a UV-Vis spectrophotometer at a wavelength of 660 nm. The inhibition percentage of BSA denaturation can be calculated by the following formula

$$\%\ \text{inhibisi} = \frac{Abs\ kontrol\ \ negatif\ -Abs\ sampel}{Abs\ kontrol\ \ negatif} \text{ x } 100\%$$

III. RESULTS AND DISCUSSION

3.1 N-octyl cinnamic/Alginate/Chitosan nanoparticlesCharacterization

The synthesis of n-octyl cinnamic in this study was obtained through an esterification reaction by reacting 0.246 mol of cinnamic acid and 2.5 mol of n-octanol using H2SO4 catalyst with the help of ultrasonic waves for 5 hours at 700C. This research refers to research conducted by [17]with a few modifications. The % yield produced is 38.31% with a melting point of 135.6-142.90C. This compound has excellent solubility in ethanol, acetone, chloroform, n-hexane, and diethyl ether. The synthesized compounds were then carried out by elucidating the structure with FTIR ATR.

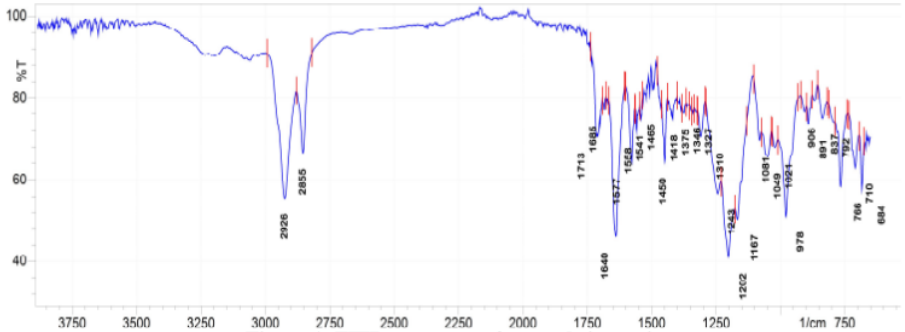
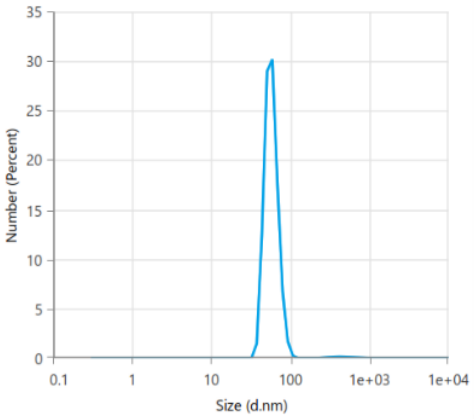


Figure 1. FTIR spectrum of n-octyl cinnamic

Nanoparticles were synthesized based on the manufacture of nanoparticle core shells. The manufacture of nanoparticles was carried out [18] with slight modifications. N-octyl cinnamate was added with sodium alginate, calcium chloride and chitosan, then stirred for 60 minutes. The reaction will produce a semi-hydrogel white colloid. Then deposited for 12 hours. Core shell nanoparticles were taken by centrifugation at 5000rpm for 20 minutes. The precipitate was dissolved in distilled water to be analyzed by a Particle Size Analyzer (PSA) to determine the particle size of the synthesized compound and the homogeneity of the particle distribution.



Name	Mean
Z-Average (nm)	519.6
Polydispersity Inde (PI)	0.5442
Intercept	0.9583
Peak 1 Mean by Intensity ordered by area (nm)	555.6
Peak 2 Mean by Intensity ordered by area (nm)	68.1
Peak 1 Area by Intensity ordered by area (%)	7.063
Peak 2 Area by Intensity ordered by area (%)	92.94
Derived Mean Count Rate (kcps)	3436
Run Used	0
Maean Count Rate (kcps)	161.5
Run Retention	100

Figure 2. Characterization of the Particle Size Analizer to determine the size of n-octyl cinnamic/Alginate/Chitosan nanoparticles

Based on the analysis of the Particle Size Analizer nano core shell n-octyl cinnamic, it can be seen that the particle size distribution shows nano size, with an average particle distribution of 40 nm, 60 nm and 90 nm. While some still show sizes > 100 nm. When viewed from the average of the data as a whole, the particles have an average of 519.6 mn. The percentage of particles is dominated by sizes less than 100 nm in terms of the peak measurement results which are at 68.1 nm. Based on the PSA analysis it also shows that the particle size is quite homogeneous, because the Poly Dispersity Index (PDI) value obtained is 0.5442 where the value is less than 0.7 [19].

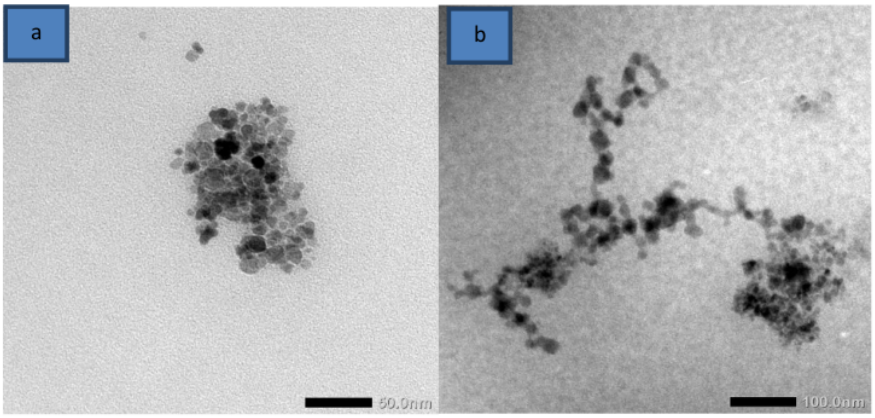


Figure 3. Scanning Electron microscopy of (a) n-octyl cinnamate (b) Core Shell n-octyl cinnamic/Alginate/Chitosan nanoparticles

TEM characterization, it can be seen that before the manufacture of n-octyl cinnamate/Alginate/Chitosan nanoparticles, the n-octyl cinnamate particles had a size smaller than 50 nm as shown in Figure 3. The synthesized N-octyl cinnamate has the property of being difficult to dissolve in polar solvents , so that in order to obtain particle distribution in polar solvents, coating or manufacture of alginate/chitosan-based nanoparticles is carried out. After coating using alginate/chitosan, it appears that the size is slightly larger with a size that is still said to be nanoparticles. The TEM results are comparable to PSA

measurements carried out previously where the particles measured by distribution in liquid solvents have a size of less than 100 nm.

Nanoparticle Adsorption efficiency

Adsorption efficiency is the amount of drug adsorbed in the nanoparticles. A good nanoparticle system is a nanoparticle that has a high adsorption efficiency. High entrapment efficiency is very beneficial because it can transport enough drug to the target cell and increases drug contact time. Observations showed that the nanoparticles produced a fairly high entrapment efficiency value of 91.02% based on the conversion carried out with the synthesized n-octyl cinnamic standard at a wavelength of 274 nm (Figure 1).

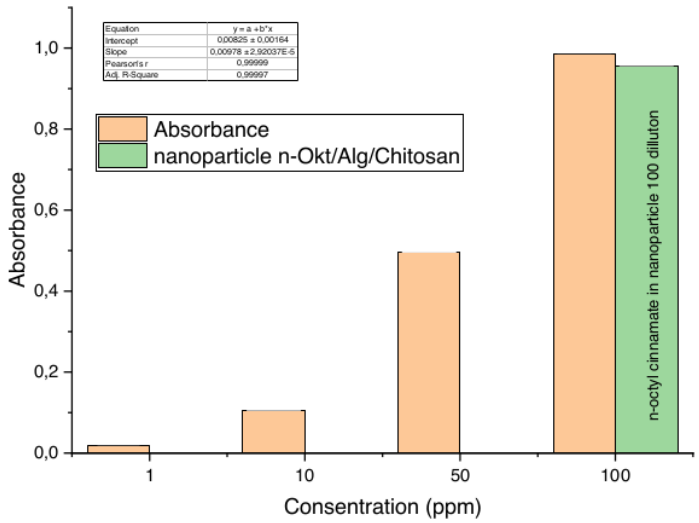


Figure 4. Calculation of % adsorption based on the standard curve of n-octyl cinnamate to n-octyl cinnamate/Alginate/Chitosan nanoparticles

Bovine Serum Albumine Anti-Inflammatory Test

Anti-inflammatory testing is based on preventing the denaturation of proteins that can be sampled. Samples prevent denaturation due to heating treatment which is carried out by incubation at extreme temperatures. The ability of the sample to prevent denaturation compared to the positive control, namely Diclofenac Na as a drug commonly used in pharmaceuticals for anti-inflammatory. Meanwhile, control was also carried out on pure n-Octyl Cinnamate to see whether the nanoparticles still had anti-inflammatory capabilities or not.

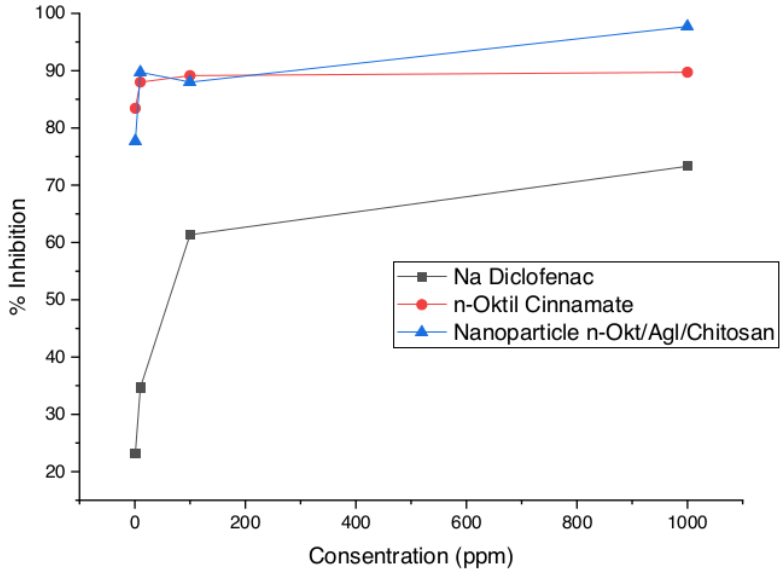


Figure 3. Anti-inflammatory activity of n-Octyl Cinnamate/Alginate/Chitosan nanoparticles

Fig. 3 can be seen that at a concentration of 1 ppm both n-octyl cinnamate and n-octyl cinnamate/alginate/chitosan nanoparticles have anti-inflammatory activity. There is a close resemblance to the synthesis of n-octyl cinnamic at a concentration of 100 ppm. Whereas at a concentration of 1000 ppm the results showed that the anti-inflammatory activity of the nanoparticles had a % higher inhibition of protein denaturation than n-octyl cinnamic. This is possible because the active compound n-octyl cinnamic is released gradually in a mechanical heating process. The slow release process results in more effective prevention of protein denaturation as in the in vitro drug delivery system. Based on the results of activity tests on n-octyl cinnamic, it can be analyzed that the replacement of the ester group (COOH) into a carboxylic group (COOR) affects its activity in inhibiting protein denaturation. The replacement of the ester group (COOH) to a carboxylic group (COOR) causes a high inhibitory effect on protein denaturation.

CONCLUSION

Synthesis of n-octyl cinnamic obtained through esterification reaction by reacting cinnamic acid and n-octanol using H2SO4 catalyst with the help of ultrasonic waves has been successfully carried out. The preparation of n-octyl cyanamate/Alginate/chitosan nanoparticles also showed success by obtaining nano-size as evidenced by the characterization of PSA and TEM. The anti-inflammatory test for both materials showed good results with a high anti-inflammatory percentage referring to the Bovine Serum Albumin method.

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REFERENCES

[1] J. D. Guzman, "Natural cinnamic acids, synthetic derivatives and hybrids with antimicrobial activity," *Molecules*, vol. 19, no. 12. MDPI AG, pp. 19292–19349, Dec. 2014, doi: 10.3390/molecules191219292.

[2] T. Vogt, "Phenylpropanoid biosynthesis," *Mol. Plant*, vol. 3, no. 1, pp. 2–20, 2010, doi: 10.1093/mp/ssp106.

[3] S. B. França, P. R. dos S. Correia, I. B. D. de Castro, E. F. da Silva Júnior, M. E. de S. B. Barros, and D. J. da P. Lima, "Synthesis, applications and Structure-Activity Relationship (SAR) of cinnamic acid derivatives: a review," *Res. Soc. Dev.*, vol. 10, no. 1, p. e28010111691, 2021, doi: 10.33448/rsd-v10i1.11691.

[4] H. S. Pawar, A. S. Wagh, and A. M. Lali, "Triethylamine: A potential N-base surrogate for pyridine in Knoevenagel condensation of aromatic aldehydes and malonic acid," *New J. Chem.*, vol. 40, no. 6, pp. 4962–4968, 2016, doi: 10.1039/c5nj03125g.

[5] L. O. Kadidae, R. Ruslin, L. Nurliana, and L. A. Kadir, "Sintesis Ester Asam Sinamat Menggunakan Variasi Katalis Asam," *J. Pijar Mipa*, vol. 15, no. 3, p. 240, 2020, doi: 10.29303/jpm.v15i3.1904.

[6] P. Volume and D. Ariastika, "Formulasi Nanopartikel Kurkumin dengan Teknik Gelasi Ionik Menggunakan Kitosan , Tripolifosfat dan Natrium Alginat serta Uji Stabilitasnya Secara In Vitro," vol. 2, no. 1, pp. 17–21.

[7] L. Pathak, T. Amrutanand, and Y. Agrawal, "Alginate-chitosan coated lecithin core shell nanoparticles for curcumin: Effect of surface charge on release properties and biological activities," *Indian J. Pharm. Educ. Res.*, vol. 51, no. 2, pp. 270–279, 2017, doi: 10.5530/ijper.51.2.32.

[8] M. Khatami, H. Q. Alijani, M. S. Nejad, and R. S. Varma, "Core@shell nanoparticles: Greener synthesis using natural plant products," *Appl. Sci.*, vol. 8, no. 3, pp. 1–17, 2018, doi: 10.3390/app8030411.

[9] N. R. P. Gofur *et al.*, "The effect of curcumin in core-shell nanoparticle as therapy in radiotherapy-induced hyposalivation," *Syst. Rev. Pharm.*, vol. 11, no. 10, pp. 367–370, 2020, doi: 10.31838/srp.2020.10.59.

[10] M. Szczęch and K. Szczepanowicz, "Polymeric core-shell nanoparticles prepared by spontaneous emulsification solvent evaporation and functionalized by the layer-by-layer method," *Nanomaterials*, vol. 10, no. 3, pp. 5–8, 2020, doi: 10.3390/nano10030496.

[11] L. F. Qi, Z. R. Xu, Y. Li, X. Jiang, and X. Y. Han, "In vitro effects of chitosan nanoparticles on proliferation of human gastric carcinoma cell line MGC803 cells," *World J. Gastroenterol.*, vol. 11, no. 33, pp. 5136–5141, 2005, doi: 10.3748/wjg.v11.i33.5136.

[12] N. Hidajati and Suyatno, "Sintesis Senyawa Tabir Matahari n-Oktil Para-Metoksi Sinamat Menggunakan Material Awal Etil Para-Metoksi Sinamat Hasil Isolasi dari Rimpang Kencur (Kaemferia galanga L .) Synthesis of a Sunscreen Compound n-Octyl Para-Menthoxy Cinnamat using Ethyl Para-M," *J. Ilmu Dasar*, vol. 9, no. 1, pp. 22–27, 2008.

[13] M. A. Arshad, U. Khurshid, S. Ahmad, S. Ijaz, F. Rashid, and R. Azam, "Review on methods used to determine Antioxidant activity," *Jezs*, vol. 1, no. 1, pp. 41–46, 2014.

[14] M. A. Oshi *et al.*, "Curcumin Nanocrystal/pH-Responsive Polyelectrolyte Multilayer Core-Shell Nanoparticles for Inflammation-Targeted Alleviation of Ulcerative Colitis," *Biomacromolecules*, vol. 21, no. 9, pp. 3571–3581, 2020, doi: 10.1021/acs.biomac.0c00589.

[15] D. Ariastika, Suryani, Wahyuni, and Rahmapiu, "Formulasi Nanopartikel Kurkumin dengan Teknik Gelasi Ionik Menggunakan Kitosan, Tripolifosfat dan Natrium Alginat serta Uji Stabilitasnya Secara In Vitro," *Maj. Farm.*, vol. 2, no. 1, p. 18, 2016, [Online]. Available: http://ojs.uho.ac.id/index.php/pharmauho/article/view/3476.

[16] K. D. P. P. Gunathilake, K. K. D. S. Ranaweera, and H. P. V. Rupasinghe, "In vitro anti-inflammatory properties of selected green leafy vegetables," *Biomedicines*, vol. 6, no. 4, pp. 1–10, 2018, doi: 10.3390/biomedicines6040107.

[17] E. Mutiara, A. Wildan, Y. D. Advistasari, E. Indriyanti, and M. Syukur, "A Green Synthesis Of N-Octyl Cinnamate By Sonochemical Method And Potential As Antioxidant And Antiinflammatory In-Vitro," vol. 12, no. 9, pp. 14–22, 2022.

[18] J. Liu, J. Xiao, F. Li, Y. Shi, D. Li, and Q. Huang, *Chitosan-Sodium Alginate Nanoparticle as a Delivery System for ε-Polylysine: Preparation, Characterization and Antimicrobial Activity*, vol. 91. Elsevier B.V., 2018.

[19] T. Mudalige, H. Qu, D. Van Haute, S. M. Ansar, A. Paredes, and T. Ingle, *Characterization of Nanomaterials: Tools and Challenges*. Elsevier Inc., 2018.

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