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Article

Nanoparticles Formulated from Young Areca Nut Extract Utilizing Sodium Alginate as a Polymer and Calcium Chloride ($CaCl_2$)

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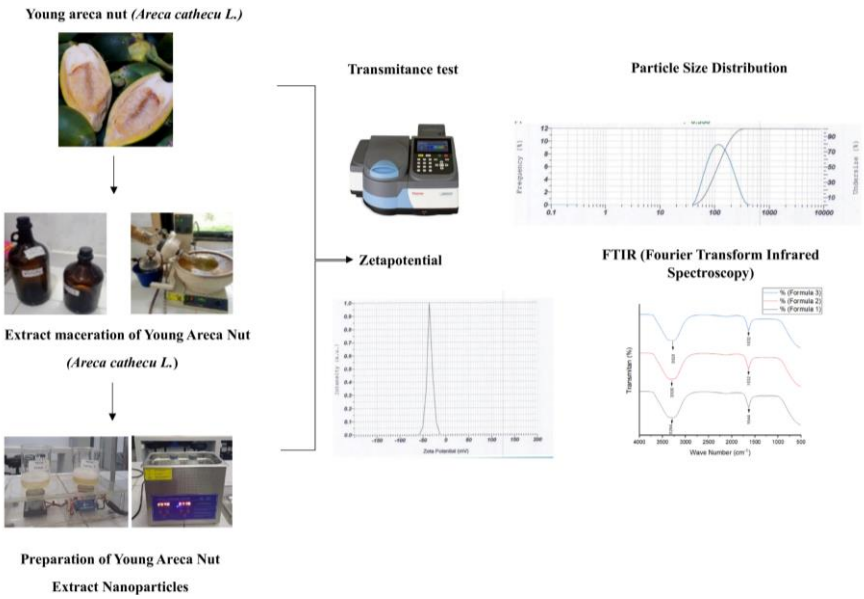
Abstract

Nanoparticles are an innovative formulation designed to enhance the bioavailability of drugs with poor absorption while allowing for a more targeted release of active compounds to minimize the risk of side effects. This study aims to develop nanoparticle formulations of young areca nut extract. The ionic gelation method, utilizing 0.02% CaCl2 and 0.1% sodium alginate, was employed in the preparation process. The three formulas were developed with different concentrations and volumes of extract. The evaluation of nanoparticles included phytochemical screening, particle size analysis (PSA), zeta potential, % transmittance, and FTIR for functional group identification. The characterization results of the nanoparticles from young areca nut seed ethanol extract showed that formulas F1, F2, and F3 had particle sizes of 84.267±1.250 nm, 97.367±1.079 nm, and 82.333±0.723 nm, respectively. The polydispersity index values ranged from 0.254±0.046 to 0.325±0.02, suggesting good particle distribution. The zeta potential values, all below -30 mV, indicate the stability of the colloidal suspension system. FTIR analysis showed that the young areca nut seed extract nanoparticles in all formulas contained functional groups such as alcohol, alkene, and amide.

Keywords: *$CaCl_2$, nanoparticles, sodium alginate, young areca nut*

Graphical Abstract



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Introduction

One of the leading and largest commodities in Jambi province is areca nut. Areca nut, also known as *Areca catechu L*., is a flowering plant that belongs to the Arecaceae family and is still one of the palmae family plants. Traditionally, areca nut seeds have been used to manufacture food, beverages, medicines, natural dyes, and cosmetics. Areca seeds are known for their therapeutic properties in health. They are used in the treatment of various conditions such as malaria, diarrhoea, vaginal discharge, skin wounds, and intestinal worms. Additionally, areca seeds are also believed to help strengthen teeth and gums [1] [2].

According to research data conducted by Fredison et al. [3], ethanol extracts from young areca nut seeds have been shown to contain various bioactive compounds, including alkaloids, flavonoids, tannins, saponins, and polyphenols, all of which possess antibacterial properties. These compounds effectively inhibit the growth of bacteria responsible for conditions like canker sores, particularly Staphylococcus aureus, with inhibition zones ranging from moderate to vigorous (6-21 mm). In addition to their antibacterial activity, young areca nut seeds demonstrate potential as antioxidants, antimutagenic agents, astringents, and antiseptics.

Developing a formulation in the form of nanoparticles can enhance the effectiveness of the delivery system for young areca nut seed extract as an antibacterial agent. Nanoparticles are an innovative preparation with the main advantage of increasing the poor bioavailability of drugs and releasing active substances that are more targeted to reduce the risk of side effects. In this case, Nanotechnology has a fast and precise drug delivery system because it has a molecular size of <1000 nm [4][5][6].

This study aims to formulate young areca nut seed extract as nanoparticles using the polymer sodium alginate (Na alginate) and calcium chloride ($CaCl_2$) as a cross-linking agent. Sodium alginate is a natural polymer and biocompatible and biodegradable material, making it safe for pharmaceutical formulations. The interaction of sodium alginate and calcium chloride can form nanoparticle preparations with good physical characteristics [7][8][9].

Material and Methods

Materials and Instrumentations

Young areca nut (*Areca catechu* L.) seeds were obtained from the Betara Sub-district, West Tanjung Jabung Regency, Jambi Province, ethanol p.a, ethanol 96%, deionized water, Na alginate, CaCl2, chloroform, $FeCl_3$, HCl, Mg and Meyer reaction. The instrumentation used in this research is magnetic stirrer (*DLAB*), blender (*Philips*), hot plate (*Cimarec+*), micropipette, petri dish, stirring rod, analytical balance (Pioneer™), FTIR (*Perkin Elmer*), Particle Size Analyzer (*Horiba Scientific SZ-100*), Vacuum rotary evaporator (*Büchi Rotavapor R-114*®), oven (*Memmert*), digital pH meter (*Hanna*), glass tools (*Pyrex*).

Methods

Preparation and Extraction. The young areca nut seeds were freshly collected, ensuring they were unripe, intact, and green in color, with the stalk still attached to the base of the fruit. The seeds were separated from the fruit's skin and sliced into thin pieces. These slices were dried in an oven at 50°C. Once dried, the material was ground into powder using a blender and sieved. Subsequently, 600 grams of the powdered material were macerated with 96% ethanol at a 1:10 ratio for 5 days. The resulting filtrate was then concentrated using a rotary evaporator to obtain a thick ethanol extract of the young areca nut seeds.

Phytochemical Screening. Young areca nut extract was identified by conducting phytochemical screening, including identifying alkaloids, tannins, flavonoids, saponins and polyphenols.

The Preparation of young areca nut extract solutions with 1, 3 and 5% concentrations. Weighed 1, 3, and 5 grams of young areca nut. Dissolve each extract with 5 ml of ethanol p.a., and add distilled water to a volume of 100.0 ml.

The preparation of nanoparticles of young areca nut extract. Young areca nut extract nanoparticles

were prepared by mixing 0.1% Na Alginate with a magnetic stirrer for 30 minutes. Then, 0.02% $CaCl_2$ was gradually added drop by drop while stirring with the magnetic stirrer. The colloid solution formed was sonicated for 1 hour. The formula of nanoparticles is shown in Table 1.

Table 1. Nanoparticle preparation formulation of young areca nut seed extract

Material	Formula (mL)		
	FI	FII	FIII
Young areca nut seed extract (1% w/v)	1	3	5
Sodium alginate (0.1% w/v)	5	5	5
$CaCl_2$ (0.02% w/v)	25	25	25

Nanoparticle Characteristics of Young Areca Nut Extract. The characteristics of nanoparticles can be evaluated by transmittance test, particle size distribution, polydispersity index test, zeta potential test, and Functional group analysis with FTIR.

Transmittance Test. The transmittance test was performed using a UV-Vis spectrophotometer with a maximum wavelength of 650 nm, and a blank aquadeion was used as the reference[10]. A higher transmittance value indicates that the particle size is decreasing [7].

Particle Size Distribution Test. Particle size determination was carried out using the Particle Size Analyser (PSA). This test is carried out by measuring particles within ± 15 minutes [4].

Polydispersity Index test. The polydispersity index describes the homogeneity of the colloidal solution. The polydispersity index has a range of values from 0 to 1. Values near 0 indicate a homogeneous dispersal, while values greater than 0.5 indicate high heterogeneity [7]. The results of the polydispersity index can meet the range of a good polydispersity index with a value range of 0.1-0.6 [8].

Zeta Potential test. Zeta potential was measured using a zeta sizer. This test is used to characterize the surface charge properties of nanoparticles. Nanoparticles with zeta potential values smaller than -30 mV and more significant than +30 mV have higher stability [7].

Functional group analysis with FTIR. The young areca nut nanoparticle extract solution was placed on the sample holder and then analyzed with an infrared spectrophotometer.

Results and Discussions

% Yield

In this stage, young areca nut seeds are oven-dried at 50°C. After drying, the simplisia is sorted and pulverized using a blender. The resulting powder from the young areca nut seeds is then extracted using the maceration method with 96% ethanol. The extract is evaporated using a rotary evaporator to obtain a concentrated extract, yielding 35.86%. The yield value can be influenced by various factors, including the solvent's polarity, the particle size of the simplisia, solvent concentration, and soaking time. Polar active compounds are more soluble in polar solvents, while nonpolar compounds dissolve better in nonpolar solvents. Choosing a solvent with the appropriate polarity for the active compounds improves extraction efficiency. Smaller particle sizes of the simplisia increase the surface area in contact with the solvent, enhancing interaction and yield. The proper solvent concentration improves the solubility of active compounds, thus increasing yield. Adequate soaking time allows the solvent to interact with the active compounds, optimizing the yield fully. The success of separating active compounds during extraction depends on the polarity or solubility differences between the active compounds and the solvent. In conclusion, optimizing factors like solvent polarity, particle size, solvent concentration, and soaking time is crucial for achieving the best extraction yield [13].

Table 2. Rendemen Extract Results

Extract	Simplisia Weight (g)	Extract Weight (g)	Yield (%)
Young Areca Nut Extract	600 g	215.20 g	35.86%

Secondary Metabolites

Young areca nut extracts were identified by conducting phytochemical screening. The content of secondary metabolites found in young areca nut seeds is listed in Table 3.

Table 3. Phytochemical Screening Results

Secondary Metaboles	Methods	Results
Alkaloids	Mayer reaction	+
Tannins	Chloroform+$FeCl_3$	+
Flavonoids	HCl+Mg	+
Saponins	Chloroform+$FeCl_3$	+
Polyphenols	Chloroform+$FeCl_3$	+

Description: (+): Positive; (-) : Negative

The results of the phytochemical screening Table 3 showed that the ethanol extract of young areca nut seeds contains alkaloids, tannins, flavonoids, saponins and polyphenols. From these results, it can be concluded that young areca nut seeds have the potential to have the ability as an antioxidant, antimutagenic, astringent, antiseptic and antibacterial[3][14][15].

Nanoparticle Characteristics of Young Areca Nut Extract.

The characteristics of nanoparticles can be evaluated by testing the percentage transmittance value, particle size distribution, polydispersity index test, zeta potential test, and Functional group analysis with FTIR.

Table 1. Results of Transmittance Test of Nanoparticles

Formulation	%Transmittance			Average±SD
	Replication I	Replication II	Replication III	
F1	91.50%	93.80%	90.70%	92±1.61
F2	85.80%	82.00%	74.40%	80.73±5.80
F3	76.50%	75.10%	67.20%	72.93±5.01

The characterization of % transmittance was carried out to observe nanoparticle formation indirectly. In general, nanoparticles have a cloudy appearance. Based on the transmittance values in Table 4, % transmittance values smaller than 100% indicate the formation of an opaque solution due to ionic interactions between Alginate and $CaCl_2$. When the calcium chloride solution interacts with the sodium alginate solution, bonds form between the Ca^{2+} ions from calcium chloride and the carboxylate groups of sodium alginate, resulting in a polyelectrolyte complex due to opposing electrostatic forces, forming an egg-box structure. The Ca^{2+} ions will bind with the guluronate acid carboxyl groups of alginate [10,16,17].

The particle size test was analyzed using a particle size analyzer. The evaluation aims to determine the particle size formed, indicated by the z average value. All of the formulation meets the nanoparticle size requirements as they fall within the 1-1000 nm range (Table 5). Formula 3 exhibits the smallest particle size. When compared to the % transmittance data in Table 4, it can be observed that higher concentrations of young areca seed extract in the nanoparticle formulation result in lower % transmittance values. However, this does not align with the particle sizes observed. Formula 3, despite having a higher extract concentration, shows the smallest particle size, which could be attributed to the effect of sonication. On the other hand, Formula 2 has the largest particle size, likely due to impurities in the young areca nut extract solution.

The polydispersity index represents the particle size distribution. A lower polydispersity index value indicates a more stable formulation, as higher values suggest that the particles are uneven in size, which can lead to quicker flocculation of the formula. The polydispersity index is close to 0.01, indicating that the formed dispersion system tends to be stable for a long time [11], [12]. The results of the polydispersity index can meet the range of a good polydispersity index, with values ranging from 0.254 – 0325 (Table 5 and Figure 1). The polydispersity index value for Formula 2 is higher

than that of the other formulas, suggesting that its particle size distribution is more varied compared to the other two formulas.

Another parameter that was analyzed is zeta potential, which is crucial for predicting the stability of colloidal dispersions. Zeta potential refers to the potential difference between the phase boundaries of solids and liquids, indicating the electric charge of particles suspended in a liquid. A high zeta potential suggests a stable formulation, as the repulsive and stabilizing forces within the nanoparticle dispersion help prevent aggregation. Conversely, a low zeta potential leads to attractive forces, which may cause the dispersion to break or flocculate. Nanoparticles with a zeta potential greater than +30 mV or less than -30 mV are typically regarded as stable colloidal suspension systems. Based on the measurement results (Table 5 and Figure 2), the zeta potential value ranges from -31.033 to -34.733 mV, indicating that the sample is stable [18][19].

Table 2. Results of Z-Avarage, PI and Zeta Potential

Formulation	Z-Average	Polydispersity Index	Zeta Potential
F1	84.267±1.250	0.258±0.091	-34.733 ±0.208
F2	97.367±1.079	0.325 ± 0.02	-32.400±0.436
F3	82.333±0.723	0.254±0.046	-31.033±1.106

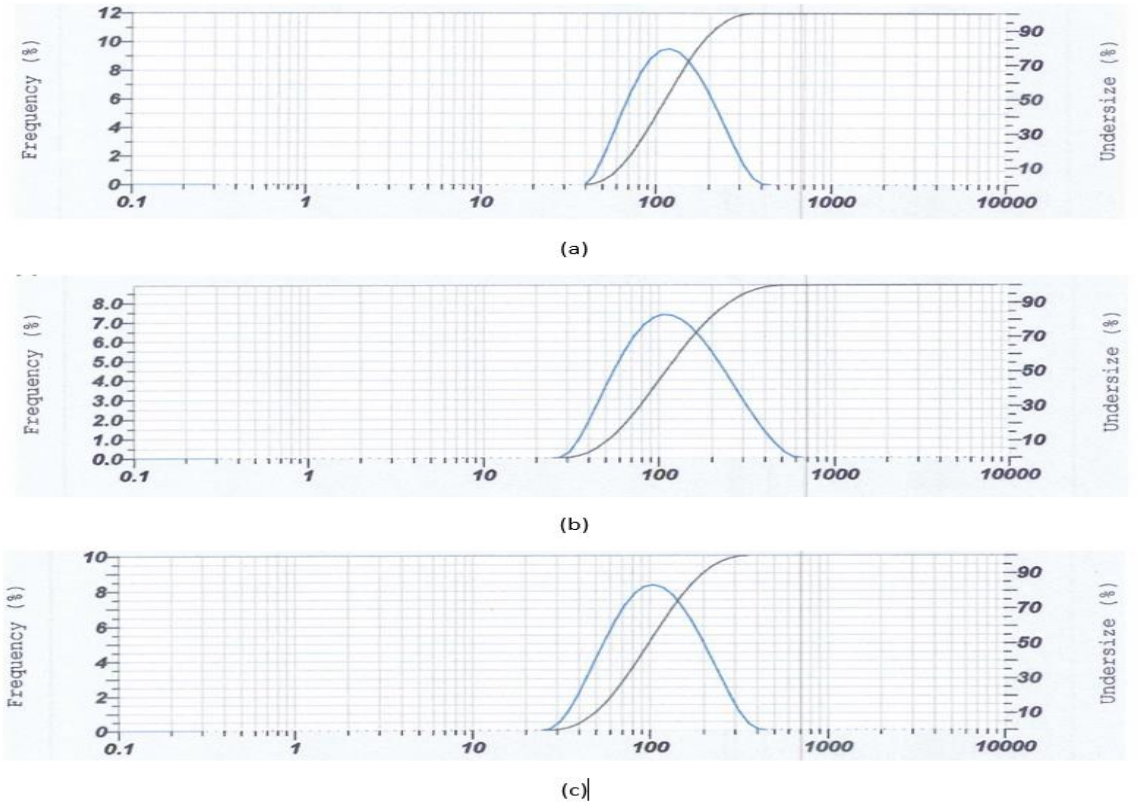

Figure 1. The particle size distribution of nanoparticles of young Areca nut. (a) Formula 1, (b) Formula 2, (c) Formula 3.

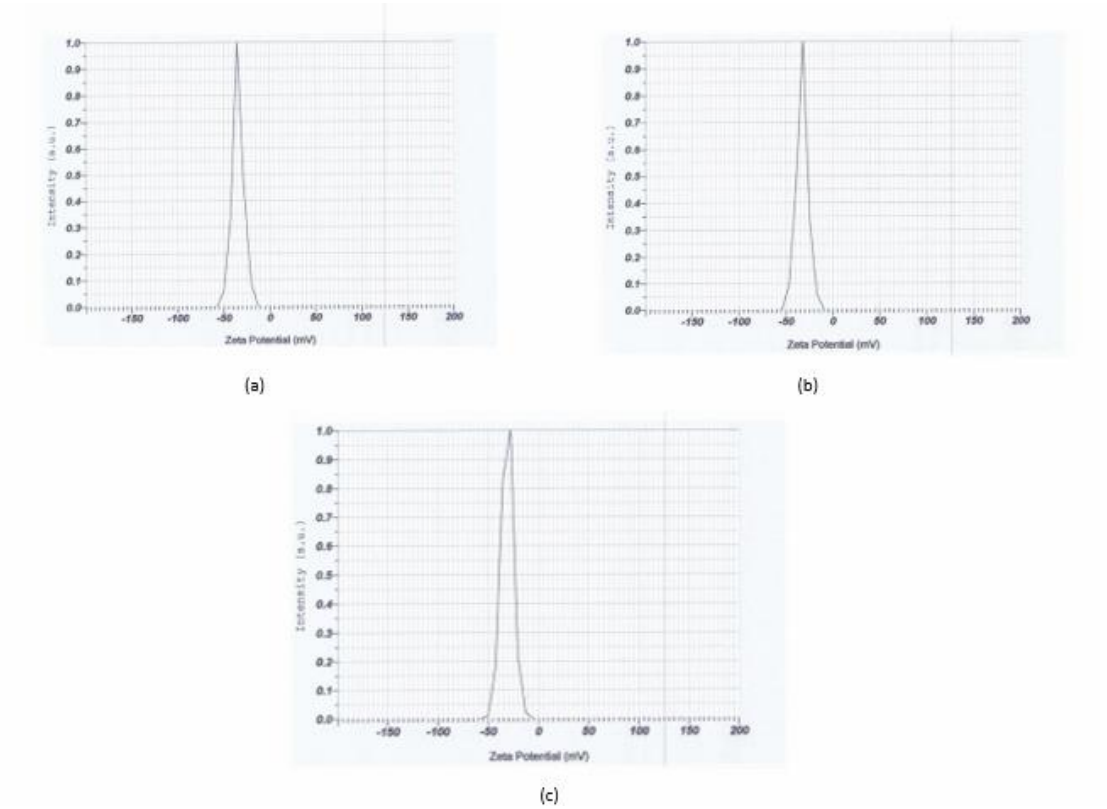

Figure 2. Zeta potential of nanoparticle young areca nut. (a) Formula 1, (b) Formula 2, (c) Formula 3.

Fourier transform infrared (FTIR) spectroscopy is an analytical technique that utilizes molecular vibrational spectra in the infrared range to characterize nanoparticles' chemical properties and molecular structure. In this case, FTIR can provide information related to chemical bonding, surface functionality, and the presence of certain compounds in nanoparticle preparations. Some aspects that can be characterized using FTIR for nanoparticles are compound identification, chemical bond analysis, surface functionality, compound purity, chemical reactions and synthesis, and phase change monitoring [20].

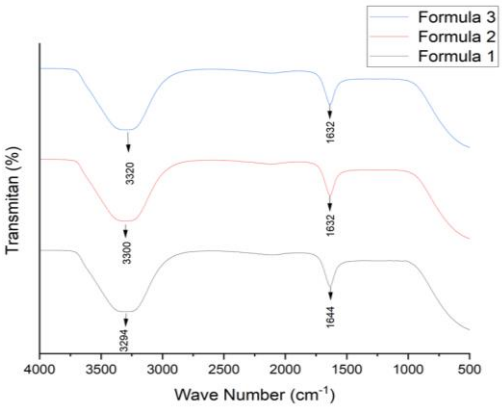

Figure 3. IR spectrum of nanoparticle formulas

This study used an FTIR (Fourier Transform Infrared) spectrophotometer to identify the functional groups contained in the ethanol extract of young areca nut seeds with their bioactive content. The following are the results of the FTIR test analysis data in Figure 3.

The functional groups observed in the 3200-3600 wavelength range correspond to alcohol hydroxyl groups (O-H). In the 1600-1680 wavelength range, the functional groups identified are alkenes with double C bonds (C=C), while at wavelengths between 1550-1640, amines and amides (N-H) are detected (Fig. 1). These results indicate that the young areca nut extract nanoparticles contain alcohol, alkene, and amide groups. Flavonoids and alkaloids, secondary metabolite compounds, can form in the presence of O-H, N-H, and C=C functional group bonds. Flavonoids typically contain structures with double bonds and hydroxyl groups, whereas alkaloids may include amine (N-H) groups and various other structures. Both flavonoids and alkaloids are known for their significant biological activities and are commonly found in a variety of plants [21].

Conclusion

The nanoparticle formulation of young Areca nut extract can be prepared using 0.1% sodium alginate as the polymer and 0.02% calcium chloride as a crosslinking agent. Formula 3 produced the smallest particle size, measuring 82.333 ± 0.723 nm, with a polydispersity index of 0.254 ± 0.046, indicating uniform particle size distribution, and was found to be stable.

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Author Contributions

Conceptualization, I. H. R. and I. M.; Methodology, I. H. R. and I. M.; Software, I. S. and A. H. N.; Validation, I. M.; Formal Analysis, Y. V. and A. H. N.; Investigation, I. H. R.; Resources, I. H. R., I. S. and E. N. B. P.; Data Curation, I. M.; Writing – Original Draft Preparation, I. H. R.; Writing – Review & Editing, I. S., I. M. and E. N. B. P.; Visualization, I. S.; Supervision, I. M.; Project Administration, I. H. R., I. S. and E. N. B. P.

Conflic of Interest

The authors declare no conflict of interest

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