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Antioxidant activity and gel formulation of Areca catechu fractionation

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Abstract

Background: Areca catechu seeds are a commodity quite common in the Sumatra area and easy to find in Jambi Province. Gel preparations are one form of preparation that can be comfortably applied to the skin's surface. The gel base is more than 60% water, making this type of preparation convenient to use as an option for cosmetic and medicinal purposes.
Method: The research was carried out experimentally, and it included plant collection, plant identification, phytochemical screening, fraction making, gel preparation formulation, antioxidant activity test using the DPPH method, and analysis of chemical components in the best fraction.
Results: The IC50 values obtained in ethanol extracts, n-hexane fractions, ethyl acetate, n-butanol, and residual water were 31.1370; 140,4038; 44,6600; 25,6350; 30,9579 µg/mL sequential. In the formulation of the gel formulation of the n-butanol fraction, the IC_{50} value at F1, F2, F3, F4, F5 is 221,9660; 73,4390; 66,1160; 114,8390; 99.3540 µg/mL sequential. Seven compounds were detected in the analysis of chemical components with HPLC-MS/MS instruments.
Conclusion: The n-butanol fraction with the best extract part in Areca catechu and F3 is the best combination of gel formulation.

Keywords: Antioxidant Activity; Areca catechu; Fractionation; Gel Formulation; IC_{50}

INTRODUCTION

The inhabitants of Jambi Province have historically relied on plant-based remedies as a form of community medicine, given their profound dependence on the natural resources found within the forest. The forest serves as a vital source of sustenance for these communities, providing not only economic benefits but also deeply rooted traditional values. The tradition of medicine in a community is inextricably linked to the local cultural context. The perception of health and the diversity of plant species utilized as traditional medicine are shaped through a socialization process that has been held to be true for generations (1–5).

The gel formulation is achieved through a process of trial and error, whereby the concentration of the gelling agent is modified until the optimal gel formula is obtained. The incorporation of gel-forming ingredients is conducted with the objective of attaining the desired characteristics of the preparation in accordance with the established specifications and criteria parameters. The utilization of diverse types and concentrations of additives and extracts will influence the physical stability of a preparation. Therefore, physical stability tests against the optimal formula are essential for gels (6–8).

Antioxidants are defined as compounds that can delay, decelerate, and prevent the oxidation process of lipids. In a particular sense, antioxidants are defined as substances that can prevent the formation of free radical reactions (peroxides) in lipid oxidation. Synthetic antioxidants, such as BHA (butylated hydroxyanisole) and BHT (butylated hydroxytoluene), have been

demonstrated to elicit significant adverse effects, including the potential for liver damage (9–11).

A free radical is defined as a compound or molecule that contains one or more unpaired electrons in its outer orbital. The presence of unpaired electrons renders the compound highly reactive, prompting it to seek out a partner by attacking and binding to surrounding electrons, thereby initiating the onset of disease (12–14).

Vitamin C is a crucial food antioxidant that markedly reduces the adverse effects of reactive species, such as oxygen radicals, which can inflict damage through oxidative reactions on macromolecules, including lipids, DNA, and proteins. These macromolecules play a role in the development of chronic diseases, such as neurodegenerative disorders. (15–17) (12–14).

The antioxidant activity of a given substance can be evaluated through in vitro testing using the DPPH (2,2-diphenyl-1-picrylhydrazile) method. The DPPH method furnishes data regarding the reactivity of the compounds under examination with a stable radical. DPPH exhibits strong absorption at a wavelength of 517 nm, resulting in a dark violet color. The action of free radical scavengers results in the pairing of electrons, which subsequently causes a proportional loss of color, contingent on the number of electrons that are taken up. (12,18,19).

METHOD

Research Time Line

The research was carried out at the Laboratory of Pharmaceutical Biology and Pharmaceutical Technology at the Health Polytechnic of the Department of Pharmacy of Jambi Province for 5 months from April to August 2024. This research consists of sampling, determination, fractionation, phytochemical compound analysis and gel formulation.

Research design

The research was conducted experimentally. This research includes plant collection, plant identification, phytochemical screening, extraction and fractionation, gel preparation formulation, antioxidant activity using the DPPH method.

Tools and Materials

1. Tool

The tools used in this research are uv-vis spectrometers, glassware, steam cups, hplc, rotary evaporators, ovens, waterbaths, analytical scales, test tubes, measuring cups, measuring flasks, filter paper, stirring rods, macerators, droppers, funnels, tweezers, parchment, containers, stationery and paper.

2. Material

The materials used in this study are sensat leaves, vitamin c, 70% ethanol, DPPH compounds, butanol, n-hexane, ethyl acetate, butanol, methanol, acetonotriel acetic acid, methanol, aqua bidestylata, Carbopol 940, propylene glycol, glycerin, methyl paraben, TEA, Aquadest.

Work Flow

1. Sampling

Sampling was carried out by Areca catechu seeds in Jambi City, Jambi Province.

2. Sample Determination

The sample used was a part of a sitting leaf obtained from Jambi. The determination of plant samples was carried out at the Taxonomy Laboratory of the Department of Biology FMIPA UNAND.

3. Extraction and Fractionation of Areca catechu

Weighed Areca catechus that have been cleaned by 5 kg, dried and then pollinated (20). Used 70% ethanol (1:10 b/v) as filter solution (21,22). Maceration is carried out 3 times and then the filtrate is concentrated until a thick extract is obtained (23,24). Subsequently the extract is fractionated with n-hexane solvent, ethyl acetate, n-butanol and residual water. 4 filtrates from 4 different fractions were obtained, then each fraction was evaporated with a rotary evaporator to obtain a viscous fraction(25–27).

4. Phytochemical tests and chemical compound analysis with HPLC-MS/MS instruments

Phytochemical analysis studies were carried out using HPLC-MS/MS instruments using. The best fractionation results were prepared by the SPE (Solid Phase Extraction) method. Furthermore, analysis with HPLC-MS/MS was carried out withsystem column type used was ACQUITY UPLC® HSS C18 (1.8 µm 2.1×100 mm, waters, USA) at temperatures of 50ºC (column) and 25ºC (room). LC analysis was used eluent A that consist of water and ammonium formate (99.9 : 0.1 ratio), and eluent B that consist of acetonitrile and formic acid (99.9: 0.1 ratio) with a flow rate of 0.2 mL/min (step gradient) for 23 min (28–32). The results of HPLC-MS/MS were then analyzed using masslynx, msconvert and sirius software (28,33–42).

5. Gel Formulation

Tabel 1. Gel Formulation

Ingredient	FI	FII	FIII	FIV	FV
Areca catechu fraction	-	0,5	1	1,5	2
Carbopol 940	1	1	1	1	1
Propylene Glycol	10	10	10	10	10
Glycerine	5	5	5	5	5
Methylparaben	0,1	0,1	0,1	0,1	0,1
TEA	1	1	1	1	1
Aquadest	ad 100 ml	ad 100 ml	ad 100 ml	ad 100 ml	ad 100 ml

The tools and materials used are prepared then a gel preparation with a Carbopol 940 base is developed in 10 parts of aquades in a mortar, left to inflate. Then TEA was added and then homogenized. Next, methyl paraben is dissolved in propyl glycol with hot distilled water at a temperature of 90°C, stirred until homogeneous. The result of fractionation of Areca catechu seeds is mixed with glycerin, mixed into the base, added to the base and stirred until homogeneous (6,43).

7. Gel Preparation Activity Test

It is made in 5 series of concentrations of 30 ppm, 40 ppm, 50 ppm, 60 ppm, and 70 ppm. Measurement of absorbance of DPPH radical reduction test solution Taken 0.2 ml each, added 3.8 ml of DPPH 35 ppm solution put into a vial and then shaken. Let stand for 30 minutes. Then the greeting is read at the maximum wavelength using a UV-vis spectrometer (17,44) (31,32). Calculation of IC50 value The concentration of the test solution to reduce 50% of free radical activity is determined by the IC50 value which can be calculated the percentage of inhibition with the formula: the results of the equation are included in the regression equation y=a+bx antioxidant activity is determined by the level of antioxidant strength based on the IC50 value (14,18,45,46).

RESULTS

The Areca catechu samples were extracted using the maceration method, then fractionation was carried out. The IC50 value in ethanol extract, n-hexane fraction, ethyl acetate, n-butanol, and residual water was 31.1370 µg/mL; 140.4038 µg/mL; 44.6600 µg/mL; 25.6350 µg/mL; 30.9579 µg/mL. Phytochemical tests were carried out by HPLC-MS/MS. 7 compounds with secondary metabolites of natural materials were obtained.

The n-butanol fraction is then formulated in the form of a gel preparation with a combination of F1-F5 with a difference in the concentration of the n-butanol fraction. Each subsequent formulation design result was calculated as the IC50 value at F1, F2, F3, F4, F5 was 221.9660 µg/mL; 73.4390 µg/mL; 66.1160 µg/mL; 114.8390 µg/mL; 99.3540 µg/mL. It was determined that F3 is the most suitable type of formula for gel formulation. However, it appears that the antioxidant activity value obtained is still not optimal, as it is lower than that of the pure fraction substance. It is anticipated that the formulation will result in enhanced antioxidant activity.

DISCUSSION

A sample was used in the form of Areca catechus (Areca catechu) obtained from Jambi province. This result will support the potential utilization of natural products native to Jambi Province for pharmaceutical and

cosmetic needs (28,47,48). The Areca catechu seeds are then extracted by maceration using a 96% ethanol solvent and then fractionated using n-hexane, ethyl acetate, n-butanol and aqua distillate solvents. Rotary evaporator is used for the concentration of the extract and fraction results obtained (20,49,50).

Tabel 2 Result

No	Molecular Weight	Formula	Compound Name	Class	Reference
1	171.19 g/mol	C8H13NO3	1-(2-Methoxyethyl)-3-methylpyrrole-2,5-diol	Alkaloid	PubChem CID 91351456
2	171.19 g/mol	C8H13NO3	(1E,3Z)-1-methoxy-4-methyl-3-nitrohexa-1,3-diene	Alkaloid	PubChem CID 117986317
3	171.19 g/mol	C8H13NO3	(2Z)-3-ethyl-5-methoxyperoxypenta-2,4-dien-1-imine	Alkaloid	PubChem CID 143200719
4	172.20 g/mol	C8H14NO3+	[(2Z)-3-ethyl-5-methoxyperoxypenta-2,4-dienylidene]azanium	Alkaloid	PubChem CID 143200718
5	199.29 g/mol	C11H21NO2	(3Z,5E)-2,6-dimethyl-8-(methylamino)octa-3,5-diene-3,4-diol	Alkaloid	PubChem CID 163735190
6	668.2 g/mol	C30H36O17	Jaceidin 7-neohesperidoside	Flavonoid	LM ID LMPK12112932
7	530.7 g/mol	C31H46O7	(1R,2R,11S,12S,14R,15R)-15-(2,6-dihydroxy-6-methyl-3-oxoheptan-2-yl)-4,14-dihydroxy-1,7,7,12,16-pentamethyltetracyclo[9.7.0.02,8.012,16]octadeca-3,8-diene-6,18-dione	Terpenoid	PubChem CID 155472242

Furthermore, the antioxidant strength of each sample that has been obtained is analyzed (14). In these results, the best potential antioxidant power was obtained in the N-butanol fraction (25.6350 µg/mL). These results show the possibility that the most dominant compound as a trigger for antioxidant power is a more polar compound with a small number of carbon atoms.

In the formulation design of the gel preparation, the best antioxidant power value was obtained in formula 3 (66.1160 µg/mL). In the results of the formulation design, a shift in IC50 value was obtained in the best fraction was the n-butanol fraction. A considerable shift in values from 25.6350 µg/mL to 66.1160 µg/mL. The results should be more optimized with a better combination of polymers. This will support changes in the value of antioxidant power for the better (27,31,51,52).

CONCLUSIONS

The conclusion obtained in this series of studies is that Areca catechu has strong antioxidant power. Areca catechus have opportunities for development, testing and treatment to be able to get the maximum potential from the original Areca catechus of Jambi province. Analysis of the results of the formulation of the best gel preparation in formulation 3 which has great potential to be further developed into nanogel form. The analysis of phytochemical results and chemical components of Areca catechus opens up opportunities for the study of Areca catechus from the perspective of in-silico testing. Alkaloids are the most dominant secondary metabolites of natural materials in this sample.

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REFERENCES

1. Ayuningtyas D, Utami RRM, Maulidya AN. The readiness of Batang Hari district as a district of human rights care: case study of the Anak Dalam tribe. Int J Hum Rights Healthc. 2020;13(3):209–17.
2. Andhika RR, Hariyadi B, Saudagar F.

Etnobotani Penghasil Getah Oleh Suku Anak Dalam Di Taman Nasional Bukit Duabelas Kabupaten Sarolangun, Jambi. J Ilmu Pertan Indones. 2015;20(1):33–8.
3. Perawati S. Traditional Plants Medicine of Suku Anak Dalam Jambi. Ris Inf Kesehat. 2017;6(2).
4. Perawati S, Andriani L, Anggresani L, Ardila E. Ethnopharmacy Study of Suku Anak Dalam (SAD) in Muara Kilis Village, Tengah Ilir, Tebo District, Jambi Province. Biospecies. 2019;12(2):36–42.
5. Yulion R, Manik F, Ulandri KR. Edukasi Penggunaan Obat Konvensional dan Obat Tradisional Berbasis Kearifan Lokal di Desa Terusan Kecamatan Maro Sebo Ilir Kabupaten Batanghari Provinsi Jambi. J Inov Pengabdi dan Pemberdaya Masy. 2022 Dec 10;2(2):217–24.
6. Sayuti NA. Formulasi dan Uji Stabilitas Fisik Sediaan Gel Ekstrak Daun Ketepeng Cina (Cassia alata L.). J Kefarmasian Indones. 2015;5(2):74–82.
7. Rinaldi R, Fauziah F, Adriani A, Silviana E, Ritazahara R. Studi Formulasi Gel Ekstrak Etanol Daun Nangka (Artocarpus heterophyllus Lam. L) dengan Basis Na-CMC dan Karbopol. J Dunia Farm. 2020;4(3).
8. Rezeki S, Endah N, Suhardiana E. Formulasi Pelembab dan Tabir Surya Alami Sediaan Gel Kombinasi Lidah Buaya dan Rumput Laut Merah. Semnaskes 2019. 2019;
9. Andriyanto BE, Ardiningsih P, Idiawati N. Skrining Fitokimia Ekstrak Daun Belimbing Hutan (Baccaurea angulata Merr.). J Jur Pendidik Kim FMIPA Univ Tanjungpura. 2016;5(4):9–13.
10. Akhtar N, Naveed M, Iqbal MZ, Khalid M, Waraich EA. Effect of consortium of plant growth promoting and compost inhabiting bacteria on physicochemical changes and defense response of maize in fungus infested soil. Pakistan J Agric Sci. 2016;53(1):59–68.
11. Sahu S, Saraf S, Kaur CD, Saraf S. Biocompatible nanoparticles for sustained topical delivery of anticancer phytoconstituent Quercetin. Pakistan J Biol Sci. 2013;16(13):601–9.
12. Mastura, Barus T, Marpaung L, Simanjuntak P. Aktivitas Antioksidan Dan Toksisitas Fraksi Etil Asetat Dari Daun Halban (Vitex Pinnata Linn) Asal Aceh. Talent Conf Ser Sci Technol. 2019;2(1):45–51.
13. Aloanis AA, Karundeng M. Total kandungan antioksidan ekstrak etanol buah beringin (Ficus benjamina Linn.). Vol. 4, Fullerene Journal of Chemistry. 2019. p. 1.
14. Rivai H, Yulion R, Krisyanella D. Penentuan Pengaruh Jenis Pelarut Pengekstrak Terhadap Perolehan Kadar Senyawa Fenolat Dan Aktifitas Antioksidan Dari Daun Jambu Biji (Psidium guajava L.). J Farm Higea. 2012;4(1):16–23.
15. Andarina R, Djauhari T. Antioksidan Dalam Dermatologi. J Kedokt dan Kesehat. 2017;4(1).
16. Supriyanto, Sari RA, Rachmawati Y, Abdullah S. Pengaruh Teknik Pengekstrakan Terhadap Kandungan Fitokimia Dan Sensoris Minuman Sirih Merah. J Teknovasi J Tek dan Inov [Internet]. 2015;02(Vol 2, No 2 (2015): Teknovasi Oktober 2015):8–14. Available from: http://ejurnal.plm.ac.id/index.php/Teknovasi/article/view/56
17. Lung JKS, Destiani DP. Uji Aktivitas Antioksidan Vitamin A, C, E dengan Metode DPPH. Farmaka. 2018;15(1).
18. Lokapur V, Jayakar V, Shantaram M. Preliminary phytochemical screening, physicochemical analysis and in-vitro antioxidant activity of selected holigarna species-endemic plant species of western ghats. Biomed. 2020;40(4):460–6.
19. Alhawarri MB, Dianita R, Razak KNA, Mohamad S, Nogawa T, Wahab HA. Antioxidant, anti-inflammatory, and inhibition of acetylcholinesterase potentials of cassia timoriensis dc. Flowers. Molecules. 2021;26(9).

20. Yulion R, Perawati S, Hartesi B, Anggresani L, Andriani L, Indriani L. Acute Toxicity LD 50 Fraction Ethyl Acetate Aquilaria Malaccensis, Ficus Benjamina, Mikania Micrantha and Fraction Water Cinnamomum Burmanii in Mus Musculus. Biol Med Nat Prod Chem. 2023;12(1):55–60.
21. Agung N. Buku Ajar: Teknologi Bahan Alam. Lambung Mangkurat University Press. 2017. 155 p.
22. Andriani L, Yulion R, Santia Manora O, Brilian Nanda R. Uji Toksisitas Akut LD50 Ekstrak Batang Bajakah Tampala (Spatholobus littoralis Hassk.) dan Batang Bajakah Kuning (Arcangelisia flava (L.) Merr.) Pada Mencit Putih (Mus musculus). Vol. 8, Medical Sains : Jurnal Ilmiah Kefarmasian. 2023.
23. Khan MAA, Islam MT. Analgesic and cytotoxic activity of Acorus calamus L., Kigelia pinnata L., Mangifera indica L. and Tabernaemontana divaricata L. J Pharm Bioallied Sci. 2012;4(2):149–54.
24. Afriani T, Yulion R, Andriani M, Syufyani F, Fadri D. The Effect of Ginger (Zingiber Officinale Roscoe) Fractionation in Decreasing Uric Acid Level of Hyperuricemic White Mice. In Scitepress; 2020. p. 467–74.
25. Liu XC, Zhou LG, Liu ZL, Du SS. Identification of Insecticidal Constituents of The Essential Oil of Acorus calamus Rhizomes against Liposcelis bostrychophila badonnel. Molecules. 2013;18(5):5684–96.
26. Rachmawaty FJ, Andianty E, Tamhid HA, Julianto TS. Antibacterial Activity of Fractions (Chloroform, Ethyl Acetate and Methanol) Red Betel Leaf Ethanol Extract (Piper crocatum) Against Streptococcus pyogenes bacteria. Int J Infect Dis [Internet]. 2019;79(2019):40.
27. Shah AJ, Gilani AH. Aqueous-methanolic extract of sweet flag (Acorus calamus) possesses cardiac depressant and endothelial-derived hyperpolarizing factor-mediated coronary vasodilator effects. J Nat Med. 2012 Jan;66(1):119–26.
28. Yulion R, Andriani L, Asadi HA, 'Aliyah SH, Mariska RP, Perawati S, et al. Spray Gel Formulation of Ethanolic Extract Senduduk Leaves (Melastoma malabatricum) Against Antioxidant Activity, SPF, and Chemical Components Analysis with LC-MS/MS. Indones J Chem Stud [Internet]. 2023 Dec 21;2(2):67–75.
29. Imran M, Rasool N, Rizwan K, Zubair M, Riaz M, Zia-Ul-Haq M, et al. Chemical composition and Biological studies of Ficus benjamina. Chem Cent J. 2014;8(1):1–10.
30. Vora A, Varghese A, Kachwala Y, Bhaskar M, Laddha A, Jamal A, et al. Eugenia jambolana extract reduces the systemic exposure of Sitagliptin and improves conditions associated with diabetes: A pharmacokinetic and a pharmacodynamic herb-drug interaction study. J Tradit Complement Med. 2019 Oct;9(4):364–71.
31. Yulion R, Andriani L, Aliyah SH. Network Pharmacology and Molecular Docking Identify the Potential Mechanism and Therapeutic Role of Scutellaria baicalensis in Alzheimer's Disease [LETTER]. Drug Des Devel Ther. 2024;18(May):1497–8.
32. Aliyah SH, Yulion R, Perawati S. Evaluations of the in vivo Laxative Effects of Aqueous Leaf and Stem Extracts of Artemisia Abyssinica in Mice [LETTER]. J Exp Pharmacol. 2024;16(April):135–42.
33. Dührkop K, Fleischauer M, Ludwig M, Aksenov AA, Melnik A V., Meusel M, et al. SIRIUS 4: a rapid tool for turning tandem mass spectra into metabolite structure information. Nat Methods. 2019;16(4):299–302.
34. Ludwig M, Nothias LF, Dührkop K, Koester I, Fleischauer M, Hoffmann MA, et al. ZODIAC: database-independent molecular formula annotation using Gibbs sampling reveals unknown small molecules. bioRxiv. 2019;(1):1–35.
35. Dührkop K, Nothias LF, Fleischauer M,

Reher R, Ludwig M, Hoffmann MA, et al. Systematic classification of unknown metabolites using high-resolution fragmentation mass spectra. Nat Biotechnol. 2021;39(4):462–71.
36. Djoumbou Feunang Y, Eisner R, Knox C, Chepelev L, Hastings J, Owen G, et al. ClassyFire: automated chemical classification with a comprehensive, computable taxonomy. J Cheminform. 2016;8(1):1–20.
37. Kim HW, Wang M, Leber CA, Nothias LF, Reher R, Kang K Bin, et al. NPClassifier: A Deep Neural Network-Based Structural Classification Tool for Natural Products. J Nat Prod. 2021;84(11):2795–807.
38. Dührkop K, Shen H, Meusel M, Rousu J, Böcker S. Searching molecular structure databases with tandem mass spectra using CSI:FingerID. Proc Natl Acad Sci U S A. 2015;112(41):12580–5.
39. Hoffmann MA, Nothias LF, Ludwig M, Fleischauer M, Gentry EC, Witting M, et al. Assigning confidence to structural annotations from mass spectra with COSMIC [Internet]. bioRxiv. 2021.
40. Böcker S, Dührkop K. Fragmentation trees reloaded. J Cheminform. 2016;8(1):1–26.
41. Böcker S, Letzel MC, Lipták Z, Pervukhin A. SIRIUS: Decomposing isotope patterns for metabolite identification. Bioinformatics. 2009;25(2):218–24.
42. Stravs MA, Dührkop K, Böcker S, Zamboni N. MSNovelist: de novo structure generation from mass spectra. Nat Methods. 2022;19(7):865–70.
43. Slamet S, Anggun BD, Pambudi DB. Uji Stabilitas Fisik Formula Sediaan Gel Ekstrak Daun Kelor (Moringa Oleifera Lamk.). J Ilm Kesehat. 2020;13(2):115–22.
44. Mukhraini. Ekstraksi, Pemisahan Senyawa, dan Identifikasi Senyawa Aktif. J Kesehat. 2021;16(2):361.
45. Castro MR, Victoria FN, Oliveira DH, Jacob RG, Savegnago L, Alves D. Essential oil of Psidium cattleianum leaves: Antioxidant and antifungal activity. Pharm Biol. 2015;53(2):242–50.
46. Maesaroh K, Kurnia D, Al Anshori J. Perbandingan Metode Uji Aktivitas Antioksidan DPPH, FRAP dan FIC Terhadap Asam Askorbat, Asam Galat dan Kuersetin. Chim Nat Acta. 2018;6(2).
47. Rizky Yulion Putra, Anggraini G, Ridha MS, Fitri N, Nurfazila N, Rahmadina R, et al. Pemanfaatan Bahan Alam untuk Pemeliharaan Kesehatan di Desa Seleman Kecamatan Danau Kerinci. Poltekita J Pengabdi Masy. 2023;4(3):693–704.
48. Mitra AD, Yulion R, Andriani M. Scientific Studies of The Activity and Acute Toxicity of LD50 Rattan As A Natural Ingredient Drug in Suku Anak Dalam (Sad) Bukit Dua Belas Jambi , Indonesia : Review Articles. Int J Pharm Sci Med. 2022;7(10):136–44.
49. Yulion R, Hadriyati A, Elvina N. Antibacterial Activity of Apple Vinegar Against the Growth of Streptococcus pyogenes. Int J Pharm Sci Med. 2023;8(6):188–91.
50. Yulion R, Yulianis Y, Suntri S. Quercetin Bioavailability Evaluation on Standardized Herbal Medicine Containing Guava Leaf Extract with HPLC. Biol Med Nat Prod Chem [Internet]. 2023 Nov 7;12(2):593–9.
51. Akhtar MS, Swamy MK. Anticancer plants: Natural products and biotechnological implements. Anticancer Plants Nat Prod Biotechnol Implements. 2018;2:1–564.
52. de Oliveira Carvalho H, Gonçalves DES, Picanço KRT, de Lima Teixeira dos Santos AVT, Lucia M, Hu X, et al. Actions of Cannabis sativa L. fixed oil and nano-emulsion on venom-induced inflammation of Bothrops moojeni snake in rats. Inflammopharmacology [Internet]. 2021 Feb 14;29(1):123–35.