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Pharmacological Activity of Plant Extracts in Self-Nanoemulsifying Drug Delivery System Dosage form: Narrative Review

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ABSTRACT: The utilization of medicinal plants as therapeutic agents has obstacles to achieving the target action due to their low solubility. Self-Nanoemulsifying Drug Delivery System (SNEDDS) is a method developed to increase the solubility of poorly water-soluble substances, such as medicinal plant extracts. This review aims to present a narrative overview of the potential utilization of SNEDDS in enhancing the pharmacological activity of plant extracts. Article searches were conducted on several websites, such as Google Scholar, PubMed, and ScienceDirect. Literature studies showed that the use of SNEDDS formulations in several medicinal plants such as dayak onion, soursop leaf, papaya leaf, bay leaf, kale, sidaguri, black cumin, mangosteen peel, harendong, pineapple peel, and cocoa is more effective than the administration of extracts alone because it can increase the solubility and bioavailability of a compound. Pharmacologically, SNEDDS shows its success in enhancing antioxidant, anti-inflammatory, analgesic, antidiabetic, antihyperglycemic, antimalarial, immunostimulant, antimicrobial, anticancer, wound healing, and hepatoprotective activities in various plant extracts. The utilization of SNEDDS formulations in plant-based drugs has a positive impact on the advancement of drug therapy, especially for compounds that have low solubility.

Keywords: **self-nanoemulsifying drug delivery system (SNEDDS); medicinal plant extracts; pharmacological activity.**

Introduction

Natural resources abound in Indonesia, both in quantity and variety. Among them is the availability of a source of plant potential that may be applied to various spheres of human endeavor, such as the medical field. Many plants found in the area offer medicinal qualities and applications that support treatment, aid in the creation of novel natural pharmaceuticals, and serve as herbal remedies when applied in accordance with empirical or scientific findings. Plant chemical composition has a direct bearing on the use of plant extracts as therapeutic ingredients [1]. The pharmacological activities of active compounds found in plant extracts, such as phenol compounds, alkaloids, flavonoids, tannins, and saponins, as well as their ability to heal wounds, stimulate the immune system, combat infection, reduce inflammation, act as antioxidants, and fight cancer, make them effective in treating various medical conditions [2,3].

Drugs can be made more soluble, absorbable, have a greater therapeutic effect, and have higher bioavailability by using the Self-Nanoemulsifying Drug Delivery System (SNEDDS). A homogenous mixture of active ingredients, surfactants, co-surfactants, and oils makes up SNEDDS formulations with dimensions between 50 and 300 nm [4]. In an attempt to produce novel herbal medications, work is currently underway to develop therapeutic plant compositions in SNEDDS preparations. Consequently, the improvement of plant extracts' pharmacological activity in the SNEDDS dosage form will be examined in this review of the literature.

Methods

In order to increase the pharmacological activity of plant extracts in the form of SNEDDS formulations, journals or original articles pertinent to all parts of the subject are gathered for this descriptive study, which employs the narrative review approach. We looked up articles using a number of services, including ScienceDirect, PubMed, and Google Scholar. Original articles published within the last ten years (2013–2023) meet the inclusion criteria; Articles with only abstracts or article reviews

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met the exclusion criteria. The terms "self-nanoemulsifying drug delivery system (SNEDDS)", "extract," "medicinal plants," and "herbal medicine" were used to search 453 articles. Twenty-five publications were used as review material for this study after the search results were chosen based on the inclusion and exclusion criteria

Result and Discussion

Self-Nanoemulsifying Drug Delivery System (SNEDDS)

Drug distribution frequently encounters the issue of drug insolubility, particularly with lipophilic medicines. Low therapeutic effectiveness and inadequate drug absorption may result from this. As a result, the Self-Nanoemulsifying Drug Delivery System (SNEDDS) was created as a technique to enhance the bioavailability and solubility of active ingredients, particularly hydrophobic molecules like plant extracts [5].

Components of The Self-Nanoemulsifying Drug Delivery System (SNEDDS)

The SNEDDS component is a homogenous mixture of oil, cosurfactant, and surfactant that, when combined with an aqueous medium and stirred, can spontaneously produce an oil-in-water nanoemulsion system [6]. When developing SNEDDS, figuring out the proportions of various components, like oil, surfactant, and cosurfactant, is crucial. Segregation is absent, and perfect mixing defines optimal SNEDDS quality. Because the physicochemical characteristics of oil, such as molecular volume, polarity, and viscosity, greatly affect a number of factors, including the process of nanoemulsification, the size of nanoemulsion droplets, drug solubility, and the biological fate of the nanoemulsion and drug, the choice of oil phase has a major influence on the formulation of SNEDDS. Oil's primary purpose is to dissolve medicine's active ingredients, whereas surfactants reduce the interfacial tension that separates water and oil. However, by decreasing the interfacial tension, improving the fluidity of the interface, and aiding in the mixing of water and oil via partitioning between the two phases, cosurfactants complement the function of surfactants [7].

Pharmacological Activity of Medicinal Plant Extracts

Plants that include components or elements that can be utilized to treat a certain illness are known as medicinal plants. All parts of plants, including leaves, flowers,

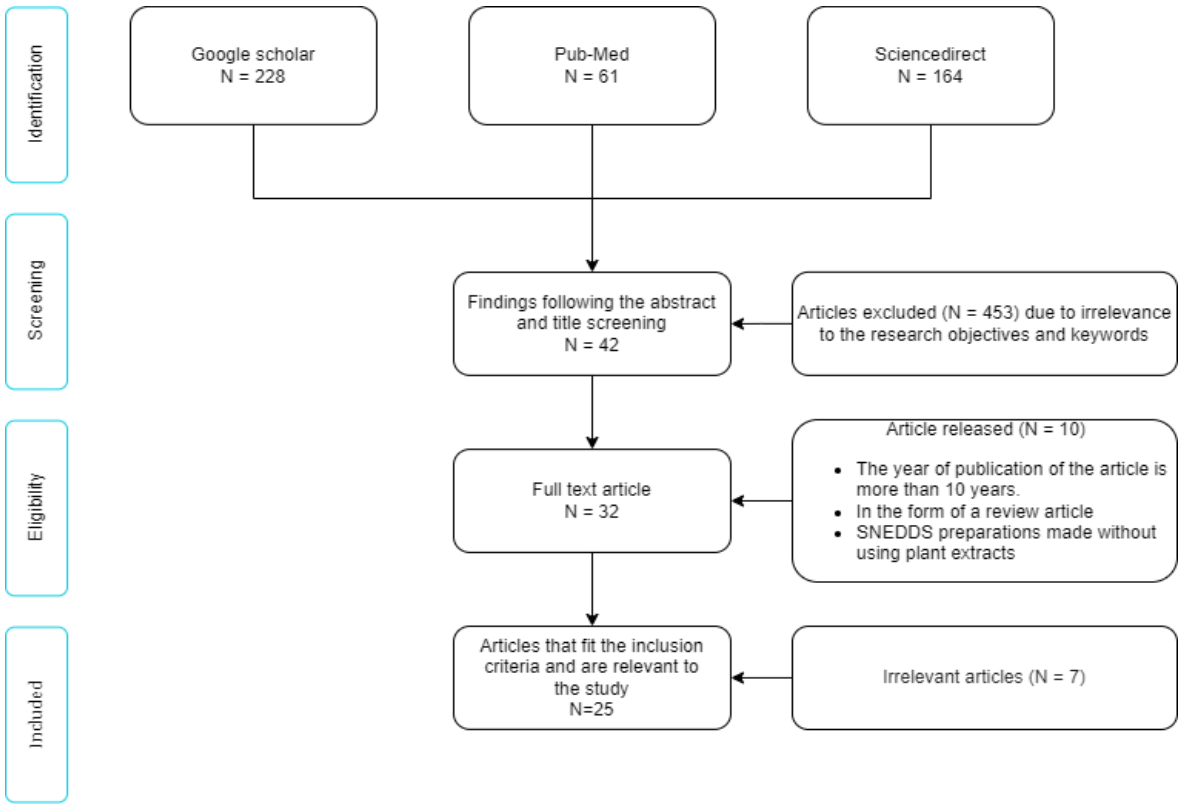

Figure 1. Flow chart for writing a review article

fruits, seeds, stems, skin, roots, and rhizomes, are used as medicines. This is because plants have pharmacological activities through the presence of active ingredients called phytochemicals, which include antioxidants, analgesics (pain relievers), antipyretics (body temperature lowering), anti-inflammatory (anti-inflammatory), and antitussive (anti-cough) [8]. Thus, it is possible to obtain naturally occurring medications that are advantageous to human health by using medicinal plants. Table 1 lists the medicinal plants that were added to SNEEDS in order to boost their pharmacological action.

Antioxidant

The test results demonstrated SNEDDS of dayak onion extract; an Inhibitory Concentration-50 (IC50) value of 38.97 ppm was found, indicating a very high level of antioxidant activity [9]. At every concentration between 10 and 60 µg/mL, the results demonstrated that Pandanus tectorius formula (PTF)-SNEDDS exhibited higher 2,2-diphenyl-1-picrylhydrazyl (DPPH) capture activity than the crude extract of Pandanus tectorius fruit. Higher antioxidant activity was attained by the crude extract becoming more soluble in aqueous solutions due to the SNEDDS formulation. An indicator of antioxidant activity is the IC50 value; the lower the IC50 value, the higher the antioxidant activity. PTF-SNEDDS showed better antioxidant activity in this investigation, as evidenced by its lower IC50 value compared to P. tectorius fruit crude extract [10]. The outcomes demonstrated that the SNEDDS formula's faloak bark extract produced optimally transparent and homogenous nano-emulsions. With an IC50 value of 70.182 ppm, the SNEDDS extract exhibits high antioxidant activity [11]. The findings demonstrated that the soursop leaf chloroform extract in the SNEDDS formulation had an IC50 value of 36.28 ppm, indicating a reasonably good antioxidant capability. The sample solution concentration required to block 50% of DPPH free radicals is known as the IC50 value; the lower the value, the higher the antioxidant activity. As a result, the soursop leaf chloroform extract SNEDDS formulation has strong antioxidant activity, as indicated by the IC50 value of 36.28 ppm [12]. The soluble characteristics of Plantago lanceolata (PL) extracts varied significantly from each SNEDDS, according to the DPPH antioxidant assay. Compared to the single extract, the diffusion efficacy of Plantago lanceolat a (PL)-SNEDDS was 4-5 times higher [13]. The study conducted by Singh [14] revealed that Eriobotrya japonica SNEDDS exhibited a higher percent inhibition of DPPH when compared to ascorbic acid. The IC50 values for both the standard and formulation were found to be 0.53 mg/ml and 0.24 mg/ml, respectively [14]. When compared to the buckwheat flavonoid suspension, the buckwheat SNEDDS preparation in vitro demonstrated a 2.2-fold greater area under the plasma concentration-time curve. The effective concentration of the nanoemulsion was assessed in vivo using the Wistar rat model. 2.6 times higher than the suspension's maximum plasma concentration (Cmax) was the SNEDDS. By improving oral bioavailability to satisfy therapeutic needs, nanoemulsion appears to be a potential oral drug delivery technology [15].

Anti-Ulcerativ Colitis

According to research, mice's colonic inflammation can be significantly reduced by the Bruceine D (BD) formulation in SNEDDS. This was accomplished by downregulating the toll-like receptor 4 (TLR4)-associated nuclear factor kappa B (NF-ϰB) transduction pathway and inhibiting oxidative damage and inflammatory mediators. Bruceine D SNEDDS considerably increased oral bioavailability and anti-colitis efficacy in comparison to BD suspension. As a result, this method offers great promise for the creation of novel medications for the treatment of ulcerativ colitis UC [16].

Analgesic

The percentage of pain inhibition in SNEDDS of papaya leaf extract reached 94.55%, according to the SNEDDS anti-inflammatory activity test performed in vivo. In contrast to suspension which employs papaya leaf extract alone and does not prepare SNEDDS at a dose of 100 mg/kgBB, it results in a pain inhibition percentage of 27.70%, whereas the best analgesic effect is achieved at a dose of 600 mg/kgBB mice, or 85.10%. Consequently, papaya leaf extract's analgesic potency may be enhanced by the delivery mechanism provided by the SNEDDS preparation [17].

Anti-Diabetic

According to the test results, there was a significant difference ($p<0.05$) in the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) values between the groups who received metformin and SNEDDS of Petiveria alliacea leaf extract and the placebo group. In streptozotocin (STZ)-induced diabetic rats, P. alliacea leaf extract SNEDDS provided greater reductions in HOMA-IR values, umor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) levels [18]. With a hypoglycemic impact of 15.6%, this study demonstrated that using SNEDDS from the ethyl acetate fraction of bay leaves might

Table 1. Pharmacological activity of plants formulated in SNEEDS preparation

Plants	Solvents of Extraction	Formula Components	Pharmacology Activity	References
Dayak Onions (*Eleutherine palmifolia*)	Ethanol	Oil: Caprylic triglyceride, Surfactants: Tween 80 & transcutol	Antioxidant	[9]
Pandanus tectorius	Hexane & methanol	Oil: caprylic triglyceride, Surfactant: Kolliphor RH40, Co-surfactant: propylene glycol	Antioxidant	[10]
Faloak (*Sterculia quadrifida* R. Br)	Ethanol	Oil: Virgin Coconut Oil, Surfactant: Tween 80, Co-surfactant: PEG 400	Antioxidant	[11]
Soursop Leaves *(Annona muricata* L.)	Chloroform	Oil: candlenut oil, Surfactant: cremophor E.L. & Tween 80, Co surfactant: propylene glycol	Antioxidant	[12]
Buckwheat (*Fagopyrum*)	-	Oil: Castor oil, Surfactant: PEG-40, Co-surfactant: Propylene glycol	Antioxidant	[15]
Java Brucea (*Brucea javanica*)	Bruceine D	Oil: Medium-chain Triglyceride (MCT), Surfactant: Solutol HS15, Co-surfactant: Propylene glycol	Anti-ulcerative colitis	[16]
Papaya Leaf (*Carica papaya* L.)	Ethanol	Oil: isopropyl myristate, Surfactant: PEG 400, Co-surfactant: Tween 80	Analgesic	[17]
Bay Leaves (*Eugenia polyantha* Wight)	Ethyl acetate fraction	Oil: Virgin Coconut Oil, Surfactant: tween 20 &/or tween 80, Co-surfactant: PEG 400	Antidiabetic	[19]
Indian Pennywort (*Centella asiatica* (L.) Urb.)	Ethanol	Oil: Capryol-90, Surfactant: Tween 20, Co-surfactant: PEG 400	Anti-hyperglycemia	[20]
Water spinach (*Ipomoea reptans*, Poir)	Ethanol	Oil: Capryol-90, Surfactan: Tween 20, Co-surfactan: PEG 400	Anti-hyperglycemia	[2]
Plantago lanceolate	Methanol	Oil: Isopropyl myristate, Surfactan: Labrasol or Kolliphor RH 40, Co-surfactan: Transcutol HP	Anti-inflammatory	[13]
Sidaguri Leaves (*Sida rhombifolia* L.)	Ethanol	Oil: Myritol 318, Surfactan: Tween 80, Co-surfactan: Propylene glycol	Anti-inflammatory	[21]
Bitter Kola (*Garcinia kola*)	Ethanol	Oil: Olive oil, Surfactan: Maisine 35-1, Co-surfactan: Cremophor EL	Antimalarial	[22]
Black Cumin (*Nigella Sativa*)	Ethanol	Oil: bottled spiny shark oil ,Surfactan: Croduret 50 ss & Tween 80, Co-surfactan: PEG 400	Immunostimulant	[23]
Propolis	Ethanol	Oil: Capryol-90, Surfactan: Cremophor RH40, Co-surfactan: PEG 400	Immunostimulant	[24]
Mangosteen (*Garcinia mangostana* L.)	Ethyl acetate fraction	Oil: Virgin Coconut Oil, Surfactan: Tween 80, Co-surfactan: PEG 400	Anti-microbial	[25]
Sarang Semut (*Myrmecodia pendans*)	Ethanol	Oil: Capryol 90, Surfactan: Tween 80, Co-surfactan: Propylene glycol	Anti-cancer	[26]
Opuntia ficus-indica L.	Hexane	Oil: OFI, Surfactan: Tween 20, Co-surfactan: PEG 200	Wound Healing	[27]
Beetroot (*Beta vulgaris* L.)	Ethanol	Oil: Linseed oil ,Surfactan: Tween 80, Co-surfactan: Propylene glycol	Hepatoprotective	[28]
Harendong *(Melastoma affine* D.DON)	Ethanol	Oil: Kollisolv, Surfactan: Tween 20, Co-surfactan: Glycerine	Hypoglycemic activity	[29]
Loquat (*Eriobotrya japonica* (Thunb.) Lindl.)	Methanol	Oil: Labrafil, Surfaktan: Tween 80, Co-surfaktan: Transcutol P	Hypoglycemic activity & Antioxidant	[14]
Pineapple peel (*Ananas comosus* L.)	Ethanol	Oil: Virgin Coconut Oil, Surfactan: Tween 80 ,Co-surfactan: PEG 400	Anti-bacterial	[32]
Salam Leaves (*Syzygium polyanthu*)	Ethanol	Oil: bottled spiny shark oil ,Surfactan: Tween 80, Co-surfactan: Propylene glycol	Anti-bacterial	[30]
Cocoa (*Theobroma cacao* L.)	Ethanol	Oil: Capryol, Surfactan: Tween 20, Co-surfactan: Propilen glikol	Anti-bacterial	[31]
Petiveria alliacea	Ethanol	Oil: Virgin Coconut Oil, Surfactan: Tween 80, Co-surfactan: polyethylene glycol	Antidiabetic	[18]

lower blood glucose levels. Moreover, in experimental animals with insulin resistance type 2 diabetes mellitus, the half-dose of SNEDDS plus metformin from the ethyl acetate fraction had a greater hypoglycemic effect (34.6%) in comparison to a single dosage of metformin (hypoglycemic effect 28.3%). These findings imply that metformin and SNEDDS bay leaf fraction combination therapy may be developed as Antidiabetic and Metabolic Regulation Improvement (ADMRI) co-therapy [19].

Anti-Hyperglycemia

Traditional medicine has advanced significantly with the creation of the SNEDDS preparation, which is made from the ethanol extract of gotu kola leaves. As zebrafish's fasting blood glucose levels decreased by 72.20% at the 200 mg/2 L SNEDDS concentration, it was found to be more effective than the 100 mg/2 L dose. The fasting blood glucose levels decreased as well, coming in at 72.20% and 69.90% for 100 mg and 200 mg of SNEDDS, respectively, according to the results of the antidiabetic activity test [20]. The antidiabetic potential of Ipomoea reptans Poir leaf ethanolic extract was investigated in this work to lower zebrafish fasting blood glucose levels. The findings demonstrated that SNEDDS of Ipomoea reptans, Poir leaf ethanolic extract, was useful in lowering blood glucose levels while fasting in zebrafish that had been given 2% glucose for seven days and 300 mg/100 ml of alloxan on the first day. A reduction of 69.03% was achieved in fasting blood glucose levels with the 200 mg/2L dose and 67.07% with the 300 mg/2L dose. These findings suggest that the ethanolic extract from the leaves of Ipomoea reptans, SNEDDS, may have potential as an antidiabetic medication for zebrafish [2].

Anti-Inflammatory

Through ear inflammation studies, the anti-inflammatory effect of the Plantago-SNEDDS combo has been demonstrated. All of the compositions were able to lessen ear edema during the course of the observation period as compared to the group that received no treatment. This suggests that plantago lanceolata (PL)-SNEDDS blends may be a reliable, effective, and secure means of delivering natural active ingredients [13]. The anti-inflammatory activity of the sidaguri leaf ethanol extract prepared by SNEDDS is greater than that of the sidaguri leaf ethanol extract solution. This is evident from the anti-inflammatory power percentage and the higher anti-inflammatory effective dose 50 (ED50) value in SNEDDS. The physical properties of SNEDDS, which have a smaller globule size than the suspension particle size, are the cause of this discrepancy [21].

Anti-Malarial

The in vivo study's data indicated that the Garcinia kola (GK) solution in SNEDDS, GK-SNEDDS suspension, and solid GK-SNEDDS formulations reduced parasite development by 77.9, 73.8, and 74.2%, respectively. At the same dose, GK-SNEDDS was found to have higher activity ($p<0.05$) than the licensed GK-based syrup (N'sansiphos®). After oral dosing, SNEDDS considerably outperformed unformulated GK and branded GK-based antimalarial syrup in terms of antiparasitic effectiveness in vivo in Plasmodium berghei-infected mice. Thus, there is a lot of potential for enhancing herbal-based malaria therapy in developing nations through the application of SNEDDS technology [22].

Immunostimulant Activity

Comparing cumin extract without formulation to SNEDDS with black cumin extract, the results demonstrated a significant increase in macrophage phagocytosis index. Nevertheless, the immunostimulating activity of black cumin extract was greater than that of cumin extract without formulation when it was made into SNEDDS using spiny dogfish oil, surfactants (Croduret 50 ss and Tween 80), and cooperative surfactant polyethylene glycol 400 (PEG 400). The findings indicated that SNEDDS with black cumin extract might raise the ratio of activated macrophages above the positive control, even if the phagocytosis index did not change significantly [23]. The findings shown that RAW 264.7 cells can be stimulated by the immunostimulatory impact of SNEDDS loaded with Propolis extract (PE) by activating the generation of nitrit oxide (NO). Tests of propolis extract's immunostimulatory activities both in vitro and in vivo revealed that propolis extract-loaded SNEDDS had greater immunostimulatory effects than propolis extract without SNEDDS. Furthermore, the production of immunostimulant activity was significantly influenced by the physical and chemical stability of SNEDDS, as well as its capacity to form emulsions [24].

Anti-Microbial

The mangosteen peel's SNEDDS Fraction Ethyl Acetate (FEA) results demonstrated antibacterial activity against Staphylococcus epidermidis, with an inhibition zone of 11.13 mm ± 1.87 mm, which was higher than the inhibition zone of 9.43 mm ± 1.20 mm for Ethyl Acetate Fraction (EAF) without formulation. Furthermore, compared to the fraction without SNEDDS, the

optimized SNEDDS from the mangosteen peel's ethyl acetate fraction exhibited greater effectiveness against S. epidermidis [25].

Anti-Cancer

The microculture tetrazolium technique assay (MTT Assay) test produced values of 258.755 ppm and 389.955 ppm, which fall into the moderately dangerous category since the IC50 is within the < 1000 ppm range, according to the data. Sarang semut (Myrcomedia pendans) SNEDDS inhibits Hela cell activity, which is how it has anticancer properties. The outcomes show that Sarang semut SNEDDS formulation inhibits Hela cell activity more effectively than the extract does [26].

Wound Healing

When rats were given traditional Opuntia ficus-indica (OFI) seed oil on day 14 after wounding, the results of OFI-SNEDDS Formula demonstrated a better healing effectiveness rate. An analysis of the Hematoxylin and Eosin (H&E) and Masson's Trichrome-stained skin through histological analysis confirmed this. Also, when compared to animals given regular OFI seed oil, OFI-SNEDDS exhibited increased anti-inflammatory and antioxidant properties. Transforming growth factor beta (TGF-β) expression was also raised along with the skin's hydroxyproline content, which was considerably boosted by both OFI and OFI-SNEDDS. Moreover, improved expression of vascular endothelial growth factor (VEGF) indicated that OFI-SNEDDS promoted angiogenesis [27].

Hepatoprotective

The formulations of Beta vulgaris L. in SNEDDS preparations were assessed in vivo and demonstrated superior potential in shielding the rats' livers from damage caused by Thioacetamide (TAA), according to the results. When compared to beet leaf (BL) extract, Formula 7 BL-SNEDDS shown a considerable improvement in liver function metrics and inflammatory markers, making it the most promising formulation. Investigations using histopathology confirmed these findings. Because it is a nano-carrier system, SNEDDS may improve the hepatoprotective effects of BL extracts [28].

Hypoglicemic Activity

The ability to lower fasting blood glucose (FBG) levels in zebrafish with diabetes mellitus to levels near normal fish FBG values was demonstrated by the SNEDDS

Table 2. Plant parts and active plant compounds that contribute to pharmacological activity in SNEDDS dosage forms

Plants	Plant Parts	Bioactive Compund	Pharmacology Activity	Literature Study
Dayak Onions (*Eleutherine palmifolia*)	Tuber	Isoliquiritigenin	Antioxidant	Strong antioxidant qualities are exhibited by isoliquiritigenin compounds due to their planarity mechanism, which influences the dissociation constant of phenolic hydroxyl groups and helps the molecule as a whole bind to the target molecule by causing electron changes in the downstream molecule. This molecule also contains a chalcone structure, which increases its antioxidant activity during the process by producing hydrogen ion radicals through the action of hydroxyl groups [35].
Faloak (*Sterculia quadrifida* R. Br)	Bark	Flavonoid dan fenolik	Antioxidant	Compounded flavonoids and phenols can shield the organism from the damaging effects of free radicals [36].
Soursop Leaves (*Annona muricata* L.)	Leaf	Flavonoid	Antioxidant	Flavonoids included in soursop leaf extract can aid in the body's defense against oxidative stress. Flavonoids protect body cells from free radical damage by directly counteracting the harmful effects of free radicals and, indirectly, by promoting the expression of endogenous antioxidant genes [37].
Buckwheat (*Fagopyrum*)	Seed	Flavonoid	Antioxidant	Buckwheat flavonoids contribute to their antioxidant properties by influencing the expression of genes and enzymes linked to oxidative stress, inflammation, and cell signaling pathways [38].
Java Brucea (*Brucea javanica*)	Fruit	Bruceine D	Anti-ulcerative colitis	In SNEDDS, Bruceine D has strong anti-inflammatory effects on colon cancerous growth via inhibiting inflammatory mediators and stres oksidatif, as well as reducing the loss of regulation from nuclear factor kappa B (NF-κB) transduksi linked to Toll-Like Receptor 4 (TLR4) [16].
Papaya Leaf (*Carica papaya* L.)	Leaf	Flavonoid	Analgesic	Flavonoids have analgesic properties because they prevent the cyclooxygenase enzyme from producing prostaglandins, which lessens pain [39].

Plants	Plant Parts	Bioactive Compund	Pharmacology Activity	Literature Study
Indian Pennywort (*Centella asiatica* (L.) Urb.)	Leaf	Flavonoid	Anti-hyperglycemia	Gotu kola contains flavonoids that have pharmacological activity, which cause blood glucose levels to drop by inducing the production of insulin by pancreatic beta cells [40].
Water spinach (*Ipomoea reptans*, Poir)	Leaf	β karoten	Anti-hyperglycemia	Antioxidant activity is exhibited by β-carotene, one of the secondary metabolite chemicals found in kale, and it also has an antihyperglycemic impact [41].
Plantago lanceolata	Leaf	Flavonoid	Anti-inflammatory & Antioxidant	Flavonoids as potent exogenous antioxidant agents [42].
Sidaguri Leaves (*Sida rhombifolia* L.)	Leaf	Flavonoid	Anti-inflammatory	The anti-inflammatory actions of flavonoids stem from their ability to inhibit the activity of cyclooxygenase (COX) enzymes, which are involved in the production of inflammatory mediators, including prostaglandins [43].
Black Cumin (*Nigella Sativa*)	Seed	Timokuinon	Immunostimulant	Thymoquinone is recognized to have immunostimulant properties, and its content is known to positively correlate with macrophages capacity to ingest latex particles. The greater the thymoquinone content, the more capable macrophages are of ingesting latex particles [44].
Propolis		Flavonoid	Immunostimulant	Through an increase in macrophage phagocytic activity, flavonoids have an immunostimulatory effect [24].
Mangosteen (*Garcinia mangostana* L.)	Fruit peel	Xanthone	Anti-microbial	The antibacterial mechanism of xanthones stems from their capacity to impede the proliferation of or eradicate germs [45].
Sarang Semut (*Myrmecodia pendans*)	Nest	Flavonoid	Anti-cancer	Flavonoids, secondary metabolites found in ant nests, have antioxidant properties that can stop the growth of cancer cells. Due to their potent antioxidant qualities, these bioactive substances may be able to inhibit the growth of cancer cells in plants, even at low concentrations [46].

formulation of harendong fruit ethanol extract at doses of 200 mg/2L and 300 mg/2L. Significant differences ($p<0.05$) were observed when compared to the control group. According to these findings, the SNEDDS ethanol extract of harendong fruit exhibits increased hypoglycemic action at that dosage, meaning that the impact is similar to that of the prescription medication metformin [29]. The in vitro alfa-amylase inhibition assay findings demonstrated that SNEDDS containing Eriobotrya japonica extract had superior antidiabetic effectiveness over standard Acarbose. This is demonstrated by the IC50 values that SNEDDS and Acarbose, respectively, obtained, which are 0.064 mg/ml and 0.091 mg/ml [14].

Anti-Bacterial

Hasil According to the findings, pure bay leaf extract was less successful than SNEDDS incorporating bay leaf extract in stopping the growth of Staphylococcus aureus germs. The size of the clear zone formed SNEDDS reached 15 mm, although the pure extract of bay leaf only reached 9 mm, indicating this [30]. The size of cocoa shell nanoparticles produced by the SNEDDS technique is smaller than that of the ionic gelation approach. Tests conducted in vitro revealed that these nanoparticles possessed a strong category of inhibition against the growth of klebsiella pneumoniae, the bacteria that causes chronic bronchitis [31]. At a dosage of 20 mg/mL, the pineapple fruit peel extract prepared by SNEDDS exhibited a high level of antibacterial strength, with an average inhibitory activity of 11.19 mm. This falls within the range of 10-19 mm, making it a strong antibacterial. The pineapple peel extract prepared via the SNEDDS method exhibits superior bacterial growth inhibition capabilities when juxtaposed with other pineapple peel extracts. Pineapple peel extract's pharmacological activity is also influenced by particle size; the smaller the particle size, the easier it is to disperse and the higher its pharmacological activity [32].

Plant Parts And Compounds Responsible For The Pharmacological Activity Of Plants In Self-Nanoemulsifying Drug Delivery System (SNEDDS) Preparations.

The pharmacological potential of plant active chemicals is enormous, and new drug delivery technologies like the Self-Nanoemulsifying Drug Delivery System (SNEDDS) have made it possible to increase the potency

and absorption of these compounds. Table 2 displays the components and plant parts that exhibit pharmacological activity.

Table 2 shows that leaves are the leaf is the component of the plant that is most heavily formed into the Self-Nanoemulsifying Drug Delivery System (SNEDDS) dosage form. This is so because leaves are the most obvious, accessible, and easily used plant organ. Leaves are the most easily processed plant-based medicinal ingredient since they can be gathered year-round and are not dependent on the season [33]. Flavonoids are the secondary metabolite substances most frequently found in plants that are prepared into SNEDDS. This is so because flavonoids are substances with a wide range of pharmacological properties, including those that are hepatoprotective, immunoregulatory, antibacterial, anticancer, antidiabetic, antimicrobial, antioxidant, and antiviral [34].

Conclusion

The Self-Nanoemulsifying Drug Delivery System (SNEDDS) is a potentially effective method for resolving medication insolubility issues, particularly for lipophilic substances like plant extracts, according to the literature study. SNEDDS can enhance the solubility and bioavailability of active ingredients by adjusting the composition of the oil phase, surfactants, and co-surfactants. SNEDDS works by forming nanoemulsions that facilitate the effective absorption of active ingredients through the gastrointestinal tract. Pharmacologically, SNEDDS demonstrated its efficacy in augmenting a range of plant extracts' antibacterial, anticancer, wound-healing, analgesic, antidiabetic, antihyperglycemic, antioxidant, and immunostimulant properties. These findings provide a solid foundation for future research and development in the field of plant-based drug formulation employing SNEDDS technology, and they positively impact the development of pharmacological therapy, particularly for poorly soluble chemicals.

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