

## Exploring the Phytochemical Properties and Therapeutic Potential of *Hibiscus sabdariffa* Linn. and *Stevia rebaudiana* Bert.

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### Abstract

Indonesian people have used medicinal plants for ages to cure various diseases. Traditional medicinal plants offer a variety of health benefits and can be an excellent alternative to prevent various diseases. Herbal tea-based treatment is low-calorie and is good for health with many benefits. Rosella (*Hibiscus sabdariffa* Linn.) and Stevia (*Stevia rebaudiana* Bert.) plants are the main composition of herbal tea. They contain various secondary metabolite compounds that play a role in pharmacological activity like alkaloids, flavonoids, phenols, glycosides, steroids, tannins, coumarins, saponins, anthraquinones, and others. This review aims to collect the latest scientific information regarding the possible pharmacological activities of Rosella and Stevia plants. These plants have antioxidative, antibacterial, antidiabetic, antihypertensive, anticancer, antihyperlipidemia, anti-obesity, hepatoprotective, anti-inflammatory, and antiprotozoal potential. PubMed, Scopus, Cochrane, ScienceDirect, and EBSCO were used to obtain literature published from 2017 to 2023. The study concludes that Rosella (*Hibiscus sabdariffa* Linn.) and Stevia (*Stevia rebaudiana* Bert.) plants have potential in the development of traditional medicinal plants with many benefits contained in them.

**Keywords:** *Hibiscus sabdariffa* Linn., *Stevia rebaudiana* Bert., pharmacology, traditional medicine

## Eksplorasi Sifat-Sifat Fitokimia dan Potensi Terapeutik *Hibiscus sabdariffa* Linn. dan *Stevia rebaudiana* Bert.

### Abstrak

Masyarakat Indonesia telah menggunakan tanaman obat sejak lama untuk menyembuhkan berbagai macam penyakit. Tanaman obat tradisional menawarkan berbagai manfaat kesehatan dan dapat menjadi alternatif yang sangat baik untuk mencegah berbagai penyakit. Pengobatan berbasis teh herbal rendah kalori dan baik untuk kesehatan dengan banyak manfaat. Tanaman Rosella (*Hibiscus sabdariffa* Linn.) dan Stevia (*Stevia rebaudiana* Bert.) merupakan komposisi utama teh herbal. Keduanya mengandung berbagai senyawa metabolit sekunder yang berperan dalam aktivitas farmakologi seperti alkaloid, flavonoid, fenol, glikosida, steroid, tanin, kumarin, saponin, antrakuinon, dan lain-lain. Ulasan ini bertujuan untuk mengumpulkan informasi ilmiah terbaru mengenai kemungkinan aktivitas farmakologis tanaman Rosella dan Stevia. Tanaman ini memiliki potensi antioksidan, antibakteri, antidiabetes, antihipertensi, antikanker, antihyperlipidemia, anti obesitas, hepatoprotektif, anti-inflamasi, dan antiprotozoa. PubMed, Scopus, Cochrane, ScienceDirect, dan EBSCO digunakan untuk mendapatkan literatur yang diterbitkan dari tahun 2017 hingga 2023. Penelitian ini menyimpulkan bahwa tanaman Rosella (*Hibiscus sabdariffa* Linn.) dan Stevia (*Stevia rebaudiana* Bert.) memiliki potensi dalam pengembangan tanaman obat tradisional dengan berbagai macam manfaat yang terkandung di dalamnya.

**Kata Kunci:** *Hibiscus sabdariffa* Linn., *Stevia rebaudiana* Bert., farmakologis, pengobatan tradisional

## 1. Introduction

Indonesia has a remarkable biodiversity, with a significant number of native medicinal plants. Recent research indicates that Indonesia possesses the second largest collection of medicinal plants globally, trailing only the Amazon rainforests. As an archipelago country, Indonesia is blessed with millions of hectares of tropical forests, which are home to thousands of plant species. Indonesia is, in fact, home to 80% of the world's medicinal plants, making it a center for traditional medicine. Indonesia's position as the world's second most biodiverse country after Brazil is an impressive feat. It is noteworthy that 15.3% of the world's total biodiversity, which is 5.1311 million, is located in Indonesia. The country's coastline spans 81,000 kilometers, equivalent to 14% of the world's sandy beaches. The Asia-Pacific region's largest tropical forests, covering 1.15 million square kilometers, are found in Indonesia. With 447 species of palms, 225 of which are endemic to Indonesia, it is quite remarkable. Indonesia's vast mangrove forests and the richest coral reefs in Asia add to the country's natural beauty.<sup>1</sup>

The Indonesian community has a long-standing tradition of using traditional medicine to treat various ailments. It is estimated that over 30 thousand traditional medicine formulas have been widely used in the country. The use of traditional medicine in Indonesia has been passed down from generation to generation and is still widely practiced today. Several plant species in Indonesia are used as traditional herbal medicines to treat various diseases, including cancer, diabetes, and hypertension. Some of the commonly used medicinal plants in Indonesia include onion, garlic, ginger, turmeric, and peppermint. Medicinal plants are considered an alternative form of therapy for enhancing health and well-being. Research shows that traditional medicine using medicinal plants is less harmful and has minimal side effects. Indonesia, a biodiversity-rich country, has an abundance of medicinal plants and plant species extensively used by the local populace. With over 5000 species of medicinal plants found in Indonesia, it is fascinating to note that their functions or

efficacy may vary in different geographical regions or ethnicities.<sup>2</sup>

Tea is a beverage that holds a special place in Indonesian culture. It is considered to be one of the most cherished and widely consumed beverages in the country. After a long day of work, many Indonesians turn to tea to help them unwind and relax. The ritual of drinking tea in the evening is often seen as an important part of daily life. In addition to traditional tea leaves, herbal teas made from various parts of plants have also become increasingly popular in recent years. The use of herbal remedies is seen as a safer and more affordable option, as it doesn't come with the caffeine and other additives that are often found in traditional tea.<sup>3</sup>

*Hibiscus sabdariffa* Linn. is known as rosella and belongs to the Malvaceae family that grows in tropical and subtropical climates. The flowers of this plant are widely used as herbal tea, which gives the tea a sour but refreshing taste.<sup>4</sup> It is known that rosella flowers contain various acids, such as citric acid, ascorbic acid, and glycolic acid, so consumers often dislike the sour taste. In addition, the sour taste produced in rosella is usually less preferred by consumers, so it becomes one of the weaknesses of rosella tea. Therefore, a material or compound containing glycosides, a complex substance containing sugar as a sweetener, is needed to reduce the sour taste of rosella tea.<sup>5,6</sup>

*Stevia* (*Stevia rebaudiana* Bert.) is a traditional medicinal plant from the Asteraceae family originating from Paraguay that grows well in tropical and subtropical climates. Stevia is an alternative sweetener to sugar cane that has several advantages, such as being natural, very sweet (200-300 times sweeter than sugar cane), has a zero glycemic index, and contains no calories, making it suitable for people with diabetes mellitus, diet, obesity, and consumers who are sensitive to synthetic sweeteners.<sup>7</sup>

This review aims to provide a comprehensive summary of the current scientific evidence on the medicinal properties of *H. sabdariffa* Linn. and *S. rebaudiana* Bert. from 2017 to 2023. The urgency of this

review arises from the growing global interest in alternative, natural therapeutic agents. As demand for herbal remedies and functional foods increases, it is essential to evaluate the pharmacological benefits of these plants in modern medicine. By synthesizing recent findings, the review identifies key knowledge gaps and highlights areas for further research. Notably, it explores the potential of combining *H. sabdariffa* and *S. rebaudiana* as herbal tea-based treatments, which may offer new therapeutic options for conditions such as hypertension, diabetes, and metabolic disorders. With the rising interest in the health benefits of these herbs, this review provides timely insights into their therapeutic efficacy, safety, and their potential as complementary or alternative treatments in global healthcare. The literature review collected from international research databases such as PubMed, Scopus, Cochrane, ScienceDirect, and EBSCO was used to identify publications that used the keywords *H. sabdariffa* Linn., *S. rebaudiana* Bert., pharmacology, and traditional medicine.

## 2. Methods

A literature review was conducted using international research databases such as PubMed, Scopus, Cochrane, and EBSCO. The review covered the period from 2017 to 2023 and aimed to identify publications that used the keywords "*Hibiscus sabdariffa* Linn.", "*Stevia rebaudiana* Bert.", "pharmacology", "medical plants", and "traditional medicine".

## 3. Result and Discussion

### 3.1. Phytochemical Profile of *H. sabdariffa* Linn. and *S. rebaudiana* Bert.

The phytochemical profile of *H. sabdariffa* Linn. and *S. rebaudiana* Bert, two popular medicinal plants, is a subject of considerable interest. *H. sabdariffa* Linn., commonly known as Roselle, is a rich source of antioxidants, flavonoids, anthocyanins, and polyphenols.<sup>8</sup> These phytochemicals are responsible for the plant's various therapeutic properties, such as anti-inflammatory, hepatoprotective, and anti-oxidative effects. Phytochemical screening shows that rosella plants (*H. sabdariffa* Linn.)

have a variety of secondary metabolite compounds, such as flavonoids, phenols, tannins, steroids, glycosides, amino acids, carbohydrates, triterpenoids, anthocyanins, quercetin, beta-carotene, delphinidin, phytosterols, hibiscetin, hibiscus, gosiperidin, and hibiscitrin.<sup>9</sup> In addition, other compounds are found in rosella flowers (*H. sabdariffa* Linn.), namely gossypetin, theaflavin, and catechin.<sup>10</sup> In addition, there is flavonoid content in rosella leaves, namely kaempferol, rutin, isoquercitrin, neochlorogenic acid, cryptochlorogenic acid, chlorogenic acid, myricetin, apigenin.<sup>11,12,13</sup> There is phenolic content in rosella, such as protocatechuic, p-coumaric, o-coumaric, and ferulic.<sup>14</sup> The roots contain phenolic compounds, and the rosella stem contains alkaloids, saponins, flavonoids, and tannins.<sup>15</sup> The fruit contains active compounds such as ascorbic acid, formic acid, acetic acid, caprylic acid, anisaldehyde, citric acid, pelargonic acid, propionic acid, benzyl alcohol, 3-methyl-1-butanol, benzaldehyde, ethanol, calcium oxalate, methanol, pectin, isopropyl alcohol, and  $\alpha$ -terpinyl acetate.<sup>10</sup>

*S. rebaudiana* Bert., also known as sweet leaf, is a natural sweetener that contains various bioactive compounds, including stevioside, rebaudioside-A (Reb-A), dulcoside-A, and rebaudioside-C (Reb-C) with stevioside compounds reported to have the highest levels of about 4-13%, and Reb-A with levels of about 2-4% based on plant dry weight.<sup>16</sup> These compounds are responsible for the plant's unique sweet taste and potential therapeutic effects, such as anti-diabetic, anti-inflammatory, and anti-hypertensive actions. Phytochemical screening shows that stevia plants (*S. rebaudiana* Bert.) have a variety of metabolite compounds, one of which is steviol glycosides, which are known to have more than 30 steviol glycoside compounds contained in stevia plants, some of which are Steviolmonoside, Rubusoside, Steviolbioside, Stevioside, Rebaudioside, and Dulcoside.<sup>17</sup> In addition, stevia leaves also contain other secondary metabolite compounds, namely alkaloids, tannins, phenolics, flavonoids, austroinulin, dulcoside, terpenoids, riboflavin, thiamin, steviol, nilacin, and beta-carotene.<sup>18</sup>

### 3.2. Pharmacological Activity of *Hibiscus sabdariffa* Linn. and *Stevia rebaudiana* Bert.

Table 1 presents a detailed summary of the pharmacological activities reported for *H. sabdariffa* Linn., while Table 2 provides an in-depth description of the pharmacological activities of *S. rebaudiana* Bert. These tables offer comprehensive information regarding the pharmacological properties of these plants, which can be useful for researchers and medical practitioners in understanding their potential therapeutic applications.

#### 3.2.1. Antioxidative

Antioxidants play a crucial role in protecting the body against the harmful effects of free radicals, which are unstable molecules that can damage cells and contribute to the development of various diseases.<sup>19</sup> The extracts were examined for their potential to scavenge free radicals using various tests, including the DPPH radical scavenging assay. The DPPH radical scavenging assay is a widely used method for evaluating the antioxidant activity of a sample. This assay measures the ability of a sample to neutralize the DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical, which is a stable radical commonly used in antioxidant assays. The DPPH radical scavenging assay is a reliable, quick, and straightforward method that can be used to assess the antioxidant potential of various natural and synthetic compounds.<sup>20</sup>

The results of the study indicate that both plant extracts possess significant antioxidative activity, due to the presence of flavonoids, phenolic, and glycoside compounds, with *Hibiscus sabdariffa* Linn. showed strong antioxidant activity with an  $IC_{50}$  value of  $46.13 \pm 3.37$  ppm. At 50  $\mu\text{g/mL}$ , the inhibition percentage was 24.1%.<sup>21</sup> *S. rebaudiana* Bert. showed strong antioxidant activity with an  $IC_{50}$  value of 48.18 ppm.<sup>22</sup> These findings suggest that these plant extracts could be used as a natural source of antioxidants with potential health benefits.

#### 3.2.2. Antibacterial

Antibacterial activity refers to the

ability of a substance to inhibit or kill bacteria. The term is commonly used in the field of microbiology to describe the effectiveness of antibiotics or other antimicrobial agents in controlling bacterial infections.<sup>23</sup> The antibacterial activity of a substance can be determined using various methods, including the Agar Well Diffusion. The Agar Well Diffusion method involves placing the substance in wells made in an agar plate that has been inoculated with bacterial strains. The substance diffuses into the agar and inhibits or kills the bacterial growth around the well, forming a zone of inhibition. The size of the zone of inhibition is measured to determine the potency of the substance against the bacterial strains tested.<sup>24</sup>

Results from recent studies suggest that the methanol extract of *H. sabdariffa* Linn. calyx exhibits higher antimicrobial activity compared to its aqueous extract. *S. rebaudiana* Bert. ethanol extract shows a strong antioxidant activity and a large zone of inhibition against *A. salmonicida*. The potential of these plants as natural remedies for bacterial infections and oxidative stress-related diseases is significant due to the presence of phenolic, flavonoid, alkaloids, saponin, tannin, and steroids compounds.<sup>25,26</sup>

#### 3.2.3. Antidiabetic

Antidiabetic activity refers to the ability of a plant or compound to help regulate blood sugar levels in people with diabetes. Diabetes is a chronic condition that affects millions of people worldwide, and it occurs when the body is unable to produce or use insulin effectively. Insulin is a hormone that is responsible for regulating blood sugar levels in the body. When blood sugar levels are not properly regulated, it can lead to a variety of health problems, such as nerve damage, kidney disease, and vision problems.<sup>27</sup>

The study conducted on the antidiabetic activity of *H. sabdariffa* Linn. revealed promising results due to the presence of flavonoids and glycoside compounds. The preparations of this plant exhibited a dose-dependent inhibition of  $\alpha$ -glucosidase activity, with an  $IC_{50}$  value of 10 mg/mL extract or 55.7

**Tabel 1.** Pharmacological Activity of *Hibiscus sabdariffa* Linn.

No.	Pharmacological Activity	Plant Part	Bioactive Compounds	Method	Result
1.	Antioxidative	Calyx	Glycoside, Alkaloid, Steroid, Triterpenoid, Tannin, and Flavonoid	DPPH (2,2-diphenyl-1-picrylhydrazyl)	The extract showed strong antioxidant activity with an $IC_{50}$ value of $46.13 \pm 3.37$ ppm. At 50 $\mu$ g/mL, the inhibition percentage was 24.1% <sup>20</sup>
2.	Antibacterial	Calyx	Flavonoid, Terpenoid, Alkaloid, Saponin, Phenolic, Anthraquinone, Tannin, and Glycoside	Agar Well Diffusion	The methanol extract of <i>H. sabdariffa</i> calyx has greater concentration-dependent antimicrobial activity (13-24 mm) compared to the aqueous extract (7-20 mm) <sup>24</sup>
3.	Antidiabetic	Calyx	Flavonoid	Spectrophotometer using p-nitrophenyl- $\alpha$ -D-glucopyranoside (In Vitro) Glucometer (In Vivo)	<i>H. sabdariffa</i> preparations inhibited $\alpha$ -glucosidase activity dose-dependently ( $IC_{50}$ = 10 mg/ml extract or 55.7 mg/mL anthocyanins) (In Vitro) <sup>27</sup> No differences were observed between hibiscus tea and hot water with white bread during the 150-minute experiment (In Vivo) <sup>27</sup>
4.	Antihypertensive	Calyx	Flavonoid and Phenolic	Animals model	The extract reduces systolic and diastolic blood pressures by 10.12% and 11.63% at 250 mg/kg body weight. It has an LD50 of 8.75 g/kg BW for male rats and 7.5 g/kg BW for female rats. It affects body weight and urea levels in male and female rats <sup>31</sup>
5.	Anticancer	Calyx	Flavonoid, Alkaloid, Saponin, and Tannin	MTT assay	The $IC_{50}$ values of 629,919 $\mu$ g/mL indicate moderate anticancer activity, with some growth inhibition observed on HepG2 cells <sup>34</sup>
6.	Antihyperlipidemic	Calyx	Flavonoid and Phenolic	Pretest-posttest approach	The R Square value of 0.143 suggests that consuming rosella steeping can affect total cholesterol levels by 14.3% <sup>37</sup>
7.	Antiobesity	Calyx	Alkaloid, Terpenoid, Steroid, Flavonoid, Tannin, Polyphenol, Coumarin, Sponin, Glycoside, and Anthraquinone	Pretest-posttest approach Enzyme-linked	Significant differences ( $p < 0.05$ ) were observed in BW, SBP, DBP, FPG, Chol, TG, HDL, LDL, NO, and cortisol levels before and after rosella administration in the treatment group <sup>40</sup>
8.	Hepatoprotective	Calyx	Phenolic	Animals model	Roselle-extract administration increased MDA levels and decreased SOD and CAT levels significantly <sup>43</sup>
9.	Anti-Inflammatory	Leaves	Flavonoid and Phenolic	Animals model	The positive control group showed 77.44% wound healing and an epithelial thickness of 49.7 $\mu$ m <sup>46</sup>
10.	Antiprotozoal	Calyx	Flavonoid and Phenolic	UHPLC-ESI-MS	Extract inhibited parasite PGR and protease activity ( $IC_{50}$ = 1.57 mg/mL and 0.76 mg/mL, respectively) <sup>49</sup>

**Tabel 2.** Pharmacological Activity of *Stevia rebaudiana* Bert.

No.	Pharmacological Activity	Plant Part	Bioactive Compounds		Method	Result
1.	Antioxidative	Leaves	Flavonoid, Glycoside	Phenolic,	DPPH (2,2-diphenyl-1-picrylhydrazyl)	The extract had the antioxidant activity ( $IC_{50} = 48.18 \mu\text{g/mL}$ ) <sup>21</sup>
2.	Antibacterial	Leaves	Phenol, Alkaloids, Steroids	Flavonoid, Saponin, Tannin,	Agar Well Diffusion	The ethanol extract had the strongest antioxidant activity ( $IC_{50} = 67.95 \mu\text{g/mL}$ ) and the largest zone of inhibition (ZOI) at 16.67 mm for <i>A. salmonicida</i> . The methanol extract had a ZOI of 15 mm at 250 mg/mL <sup>25</sup>
3.	Antidiabetic	Leaves	Glycoside		Animals model	The positive control results decreased significantly ( $P < 0.01$ ) from $278.63 \pm 3.35 \text{ mg/dL}$ on day 0 to $125.02 \pm 2.09 \text{ mg/dL}$ on day 60 <sup>28</sup>
4.	Antihypertensive	Leaves	Glycoside		Randomized cross over placebo-controlled study	The systolic BP increased following stevia intake from $114.5 \pm 12.7$ to $119.9 \pm 12.9 \text{ mmHg}$ ( $p < 0.001$ ) and diastolic BP from $70.8 \pm 9.4$ to $75.7 \pm 9.6 \text{ mmHg}$ ( $p < 0.01$ ) <sup>32</sup>
5.	Anticancer	Leaves	Alkaloid, Flavonoid, Triterpenoid	Saponin, Tanin,	MTT assay	Stevia leaf extract demonstrated an $IC_{50}$ value of $511.07 \mu\text{g/mL}$ on HeLa cells <sup>35</sup>
6.	Antihyperlipidemic	Leaves	Glycoside		Animals model	The HDL level in hyperlipidemic rats was improved from $39.76 \pm 4.34$ to $42.02 \pm 4.39 \text{ mg/dL}$ <sup>38</sup>
7.	Antiobesity	Leaves	Glycoside		Pancreatic lipase and alpha-amylase inhibitory activity using quantitative plate assay	The methanolic extract inhibited pancreatic lipase with an $IC_{50}$ of $5.74 \mu\text{g/mL}$ , similar to a well-known anti-obesity drug <sup>41</sup>
8.	Hepatoprotective	Leaves	Glycoside, Sesquiterpenoid	Flavonoid,	Animals model	Liver tissue molecular profiling showed reduction in elevated TNF- $\alpha$ by 23.83%, 29.06%, 28.34% <sup>44</sup>
9.	Anti-Inflammatory	Leaves	Glycoside		Molecular docking	$\beta$ -sitosterol, campesterol, and stigmasterol exhibited high affinity to COX-1, COX-2, and 5-LOX. The free energy of binding value was -11.12, -11.43, and -10.62 kcal/mol for COX-1, -11.45, -11.34, and -11.84 kcal/mol for COX-2, and -5.95, -11.34, and -9.08 kcal/mol for 5-LOX <sup>47</sup>
10.	Antiprotozoal	Leaves	Glycoside, Saponin		In vitro batch cultures	Extract promoted a linear decrease ( $P < 0.001$ ) in protozoa activity <sup>50</sup>



mg/mL anthocyanins. The study also observed that there were no significant differences between hibiscus tea and hot water with white bread during the 150-minute experiment. In comparison, the positive control results of *S. rebaudiana* Bert. decreased significantly ( $P < 0.01$ ) from  $278.63 \pm 3.35$  mg/dL on day 0 to  $125.02 \pm 2.09$  mg/dL on day 60. These findings suggest that *H. sabdariffa* Linn. and *S. rebaudiana* Bert. has the potential to be an effective natural alternative for managing diabetes.<sup>28,29</sup>

#### 3.2.4. Antihypertensive

Antihypertensive activity pertains to the capacity of a substance to regulate or lower high blood pressure levels. This ability may be displayed by either natural or synthetic compounds that have been demonstrated to decrease blood pressure in clinical or preclinical research. Antihypertensive agents function by expanding blood vessels, lessening blood volume, or blocking certain enzymes or hormones that regulate blood pressure.<sup>30</sup>

According to a recent study, *H. sabdariffa* Linn. and *S. rebaudiana* Bert. have been found to possess significant antihypertensive activity due to the presence of flavonoids, phenolic, and glycoside compounds. Specifically, *H. sabdariffa* Linn. extract has demonstrated antihypertensive activity by reducing systolic and diastolic blood pressures by 10.12% and 11.63% at a concentration of 250 mg/kg body weight, respectively. However, it should be noted that its  $LD_{50}$  is 8.75 g/kg BW for male rats and 7.5 g/kg BW for female rats. Moreover, the extract affects body weight and urea levels in both male and female rats. Similarly, *S. rebaudiana* Bert. has been found to increase systolic blood pressure from  $114.5 \pm 12.7$  to  $119.9 \pm 12.9$  mmHg ( $p < 0.001$ ) and diastolic blood pressure from  $70.8 \pm 9.4$  to  $75.7 \pm 9.6$  mmHg ( $p < 0.01$ ) upon intake.<sup>31,32</sup>

#### 3.2.5. Anticancer

Anticancer activity is a term that denotes the ability of a substance or a treatment to prevent the uncontrolled growth and spread of malignant cells in the body. It is a multifaceted activity that can manifest in various forms,

such as inhibiting angiogenesis (the formation of new blood vessels), inducing apoptosis (programmed cell death), or interfering with the cancer cell's mitotic machinery, which controls its ability to divide and proliferate.<sup>33</sup>

A recent study has revealed that *H. sabdariffa* Linn. and *S. rebaudiana* Bert. have potential anticancer properties due to the presence of flavonoid, alkaloid, saponin, and tannin compounds. In particular, *Hibiscus sabdariffa* Linn. extract has been observed to possess moderate anticancer activity, with some growth inhibition noticed on HepG2 cells, as evidenced by the  $IC_{50}$  values of 629,919  $\mu$ g/mL. Similarly, *S. rebaudiana* Bert. has demonstrated anticancer activity with an  $IC_{50}$  value of 511.07  $\mu$ g/mL on HeLa cells. These findings indicate that these natural compounds may have therapeutic potential in the development of new anticancer drugs.<sup>34,35</sup>

#### 3.2.6. Antihyperlipidemic

Antihyperlipidemic activity refers to the ability of a substance or medication to reduce the levels of lipids (fats) in the blood. This includes reducing levels of cholesterol, triglycerides, and other types of lipids that can contribute to the development of cardiovascular disease. These antihyperlipidemic work by inhibiting the synthesis of lipids in the liver, increasing the breakdown and elimination of lipids from the body, or interfering with the absorption of lipids from the diet.<sup>36</sup>

According to a recent study, both *H. sabdariffa* Linn. and *S. rebaudiana* Bert. have been found to possess potential antihyperlipidemic properties, which can be attributed to the presence of flavonoid, phenolic, and glycosides compounds. More specifically, the extract of *H. sabdariffa* Linn. has been observed to exhibit moderate antihyperlipidemic activity, with the R Square value of 0.143 indicating that the consumption of rosella steeping can significantly affect total cholesterol levels by 14.3%. On the other hand, *S. rebaudiana* Bert. has also been found to demonstrate antihyperlipidemic activity, as evidenced by the improvement in HDL levels in hyperlipidemic rats from  $39.76 \pm 4.34$  to  $42.02 \pm 4.39$  mg/dL. These findings suggest

that both *H. sabdariffa* Linn. and *S. rebaudiana* Bert. have the potential to be used as natural remedies for managing hyperlipidemia.<sup>37,38</sup>

### 3.2.7. Antiobesity

Antiobesity activity refers to the property of a substance or compound to prevent or reduce obesity, which is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health. Substances with antiobesity activity may work by suppressing appetite, increasing metabolism, reducing the absorption of fats or carbohydrates, or promoting the breakdown and elimination of fats.<sup>39</sup>

A recent study has conducted research on the anti-obesity properties of two plant species, namely *H. sabdariffa* Linn. and *S. rebaudiana* Bert. The study has found that these plants contain a variety of compounds such as alkaloid, terpenoid, steroid, flavonoid, tannin, polyphenol, coumarin, saponin, glycoside, and anthraquinone that have potential anti-obesity properties. The research has revealed that the extract of *H. sabdariffa* Linn. has a moderate level of anti-obesity activity. The study has observed significant differences ( $p < 0.05$ ) in the levels of various parameters such as body weight (BW), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (FPG), cholesterol (Chol), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), nitric oxide (NO), and cortisol levels before and after treatment with *Hibiscus sabdariffa* Linn. extract. Similarly, the research has shown that *S. rebaudiana* Bert. also possesses anti-obesity activity. The methanolic extract of *S. rebaudiana* Bert. has demonstrated an ability to inhibit pancreatic lipase with an  $IC_{50}$  of 5.74  $\mu\text{g/ml}$ , which is comparable to a well-known anti-obesity drug.<sup>40,41</sup>

### 3.2.8. Hepatoprotective

Hepatoprotective activity refers to the ability of a substance or compound to protect the liver from damage caused by toxins, chemicals, and other harmful agents. It is the ability of a substance to maintain the normal functioning of the liver and prevent liver

disorders. Hepatoprotective agents are often used to prevent and treat liver diseases such as hepatitis, cirrhosis, and fatty liver. These agents work by various mechanisms such as reducing oxidative stress, inflammation, and apoptosis, enhancing liver regeneration, and promoting the secretion of bile.<sup>42</sup>

According to a recent study, it has been found that *H. sabdariffa* Linn. and *S. rebaudiana* Bert. have the potential to exhibit hepatoprotective properties. These properties are attributed to the presence of various compounds such as phenolic, glycoside, flavonoid, and sesquiterpenoid in both the herbal extracts. In particular, the extract obtained from *H. sabdariffa* Linn. has been observed to possess moderate hepatoprotective activity. Roselle-extract administration has been found to increase MDA levels, which is a marker of oxidative stress, and decrease SOD and CAT levels significantly. These enzymes are responsible for combating oxidative stress and their reduced levels indicate the potential of *Hibiscus sabdariffa* Linn. extract in protecting liver cells from oxidative damage. Similarly, *Stevia rebaudiana* Bert. has also demonstrated hepatoprotective activity. The molecular profiling of liver tissue has shown a reduction in elevated TNF- $\alpha$  by 23.83%, 29.06%, and 28.34%. TNF- $\alpha$  is a pro-inflammatory cytokine that is produced in response to liver damage. The reduction in TNF- $\alpha$  levels indicates that *Stevia rebaudiana* Bert. may have the potential to reduce liver inflammation.<sup>43,44</sup>

### 3.2.9. Anti-Inflammatory

Anti-inflammatory activity refers to the ability of a substance to reduce inflammation in the body. Inflammation is a natural response of the immune system to injury or infection, but chronic inflammation can lead to several health problems, including autoimmune disorders, cardiovascular diseases, and cancer. Therefore, substances with anti-inflammatory activity are considered beneficial for preventing or managing such health problems. These substances work by reducing the production of pro-inflammatory cytokines, blocking the activity of enzymes that promote inflammation,



or enhancing the activity of anti-inflammatory molecules.<sup>45</sup>

According to a recent study, it has been discovered that *H. sabdariffa* Linn. and *S. rebaudiana* Bert. contain flavonoid, phenolic, and glycosides compounds that have potential anti-inflammatory properties. The study particularly highlights the moderate anti-inflammatory activity of *H. sabdariffa* Linn. extract, which was observed to exhibit a 77.44% wound healing rate and an epithelial thickness of 49.7  $\mu\text{m}$  in the positive control group. On the other hand, *S. rebaudiana* Bert. has also demonstrated anti-inflammatory activity, with  $\beta$ -sitosterol, campesterol, and stigmasterol exhibiting a high affinity to COX-1, COX-2, and 5-LOX. The free energy of binding value for COX-1 was -11.12 kcal/mol, while for COX-2 it was -11.45 kcal/mol, and for 5-LOX it was -5.95 kcal/mol. These findings suggest that both *H. sabdariffa* Linn. and *S. rebaudiana* Bert. have the potential to be used in treating inflammation-related conditions.<sup>46,47</sup>

#### 3.2.10. Antiprotozoal

Antiprotozoal activity refers to the ability of a substance to inhibit or kill protozoa, which are single-celled organisms that can cause various diseases in humans and animals. Protozoa are responsible for diseases such as malaria, giardiasis, leishmaniasis, toxoplasmosis, and amoebiasis, among others. Antiprotozoal substances work by interfering with the metabolism, replication, or other vital functions of the protozoa, leading to their death or inhibition of growth.<sup>48</sup>

A recently conducted research study has uncovered some promising antiprotozoal properties associated with two plant species - *H. sabdariffa* Linn. and *S. rebaudiana* Bert. The study found that these plants contain several compounds like flavonoid, phenolic, saponin, and glycosides that are responsible for their antiprotozoal activity. The study further revealed that the extract derived from *H. sabdariffa* Linn. possesses moderate antiprotozoal activity. The extract was observed to inhibit parasite PGR and protease activity, with  $\text{IC}_{50}$  values of 1.57 mg/

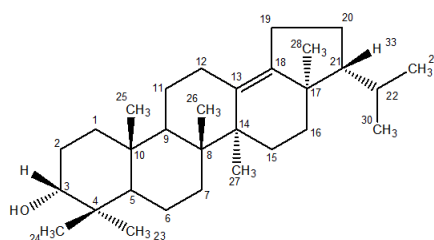
mL and 0.76 mg/mL, respectively. Similarly, *S. rebaudiana* Bert. also showed promising antiprotozoal activity. The extract obtained from Stevia promoted a linear decrease (with  $P < 0.001$ ) in protozoa activity, which indicates its potential to combat protozoal infections. These findings highlight the potential of *H. sabdariffa* Linn. and *S. rebaudiana* Bert. as natural sources of antiprotozoal agents that can be utilized for the development of new therapeutic agents against protozoal infections.<sup>49,50</sup>

#### 4. Conclusion

This review highlights the therapeutic potential of *H. sabdariffa* Linn. and *S. rebaudiana* Bert., which demonstrate various health benefits. Phytochemical compounds present in these plants, such as flavonoids, phenolics, and glycosides, are responsible for their therapeutic effects. The review aims to support the development of safe, affordable, and effective natural treatments for various health conditions. The findings suggest these plants could contribute to the creation of new herbal medicines, offering valuable treatment options for numerous health issues.

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**Gambar 2.** Struktur kimia isolat (neohope-13(18)-ene-3 -ol)

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