

## Phytochemical and Potential Antidiabetic of *Catharanthus roseus*: A Review

**Resty Apriliani<sup>1</sup>, Widya Kardela<sup>1</sup>, Fitra Fauziah<sup>1\*</sup>**

<sup>1</sup>Department of Pharmacology and Clinical Pharmacy, School of Pharmaceutical Science (STIFARM) Padang, West Sumatera, Indonesia, 25147

### **Abstract:**

**Background:** Diabetes as a global problem increases in prevalence worldwide. Treatment of diabetes mellitus currently uses synthetic drugs. As we know, synthetic drugs have many side effects. Therefore, some people use herbal medicine as an alternative to treat diseases. One of them is *Catharanthus roseus*. This plant is a herbal medicine that has the potential as antidiabetic.

**Material and Methods:** This article reviews the phytochemical compounds and in vivo and in vitro antidiabetic activity testing of *Catharanthus roseus* in the last decade. Three bibliographic databases were used as sources of information (PubMed, ScienceDirect, and Google Scholar). The keywords used in this literature search were "Antidiabetic," "Pharmacology," "Phytochemical," and "*Catharanthus roseus*."

**Results:** There are 22 articles in this review based on the eligibility criteria. It was divided into nine phytochemical literature studies and 13 antidiabetic literature studies.

**Conclusion:** Pharmacological studies reported that *Catharanthus roseus* could lower blood glucose levels and is an herbal treatment for antidiabetics.

**Keywords:** antidiabetic; *Catharanthus roseus*; pharmacology; phytochemical

### **I. Introduction**

Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The development of diabetes starts from autoimmune destruction of pancreatic beta cells, then insulin deficiency, to disorders that cause insulin resistance. Abnormal metabolism of carbohydrates, fats, and proteins is the effect of insufficient insulin on target tissues. This insulin deficiency is caused by insufficient secretion or weak tissue response to insulin<sup>1</sup>.

Based on the cause, Diabetes Mellitus (DM) can be classified into four groups: type 1 DM, type 2 DM, gestational DM, and other types of DM. Type 2 diabetes is the most common type of diabetes because various epidemiological studies tend to increase the incidence and prevalence of type 2 diabetes in various parts of the world<sup>2</sup>.

Diabetes as a global problem increases in prevalence yearly in the world and Indonesia. Based on data from the International Diabetes Federation (IDF), the prevalence of diabetes worldwide in 2021 will be 537 million adults (20-79 years old) living with diabetes. This number was expected to increase to 643 million by 2030 and 783 million by 2045. According to the World Bank Income classification, the number of people with diabetes in high-income countries is 103.9 million, middle-income countries are 414.0 million, and low-income countries are 18.7 million. Diabetes will cause 6.7 million deaths in 2021<sup>3</sup>.

Treatment of DM currently uses synthetic drugs. As we know, synthetic drugs have many side effects, such as the potential side effect of nausea on using Metformin and Glimepiride. Glibenclamide can cause side effects of hypoglycemia<sup>4</sup>. Previous studies also mentioned that DM is a degenerative disease, so the drugs given must be consumed regularly and continuously, even for a lifetime, because degenerative diseases can directly affect the decline in kidney conditions in diabetic nephropathy patients<sup>5</sup>.

## Phytochemical and Potential Antidiabetic of *Catharanthus roseus*: A Review

*Catharanthus roseus* (Apocynaceae) is a plant native to the Indian Ocean Island in Madagascar. *Catharanthus* comes from the Greek word meaning "pure flower." In contrast, *roseus* means red, rose, or rosy<sup>6</sup>. *C.roseus* is known to have pharmacological activities such as antidiabetic<sup>7</sup>, antioxidant<sup>8</sup>, antibacterial<sup>9</sup>, anticancer<sup>10</sup>, antitumor<sup>11</sup>, wound healing<sup>12</sup>, and antihyperlipidemic<sup>13</sup>.

However, only a few tests for the phytochemical content and potential as antidiabetic have been carried out on *C.roseus*. This literature review aims to collect and summarize current knowledge about the phytochemical and antidiabetic activity of *C.roseus* from in vitro and in vivo studies published since 2011.

## II. Methods

The method used by researchers in writing this review article is a literature review study. This review includes searches conducted from 3 scientific literature databases: PubMed, ScienceDirect, and Google Scholar. A search and collection of literature were carried out from 2011 to 2021, which discussed the phytochemical and antidiabetic activity of *Catharanthus roseus* in vivo or in vitro. The keywords used in this literature search were "Antidiabetic," "Pharmacology," "Phytochemical," and "*Catharanthus roseus*." All abstracts and complete articles were collected, examined, summarized, and concluded. The selected articles are the most relevant and included in this article review.

## III. Result

Based on the results of article screening from Figure 1, the obtained 22 articles are used, as shown in Tables 1 and 2.

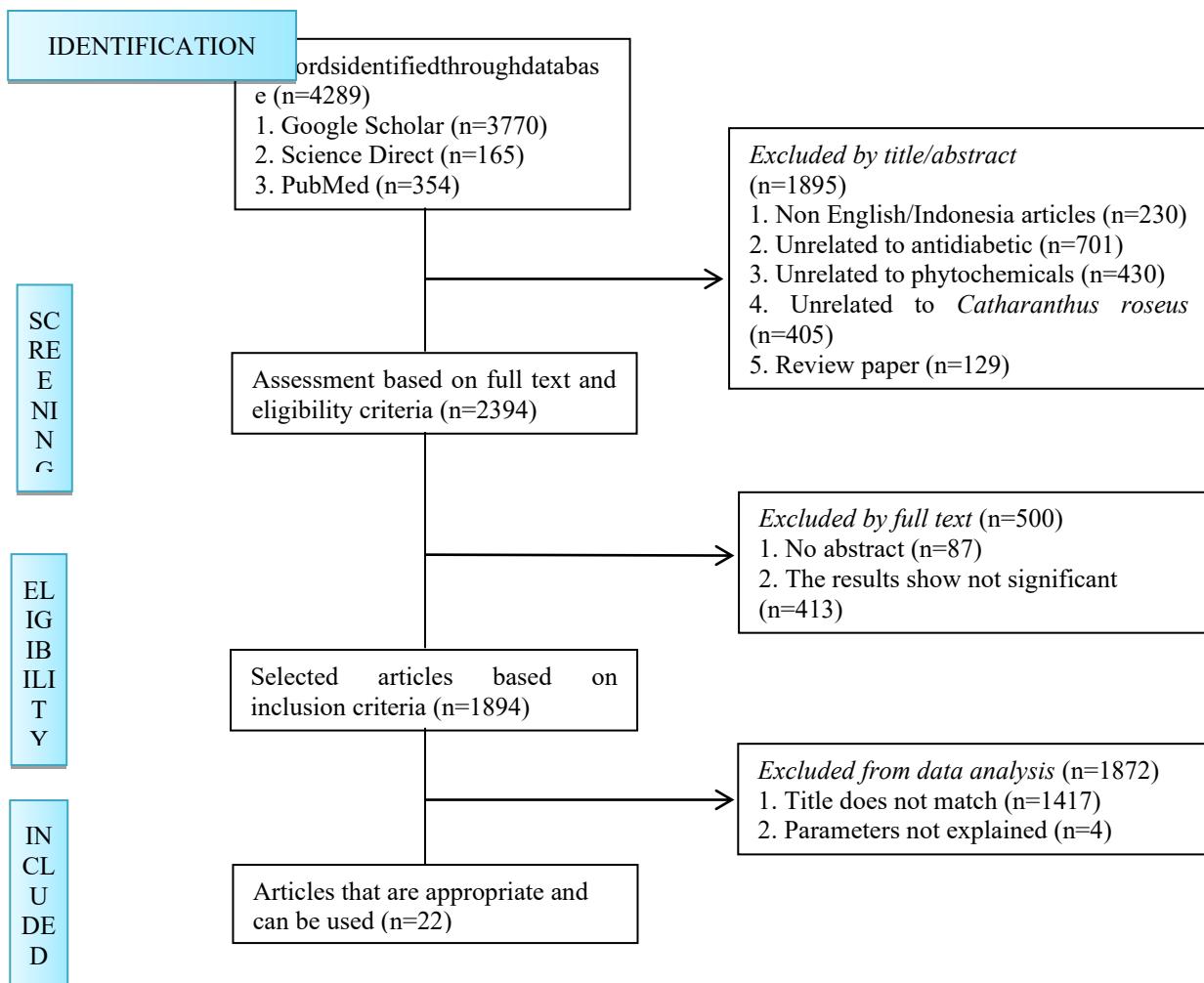


Figure 1. PRISMA Flowchart of Literature Search

The comprehensive literature study on phytochemicals and antidiabetic *Catharanthus roseus* were 22 articles. It was divided into nine phytochemical literature studies and 13 antidiabetic literature studies.

### **Phytochemicals**

The phytochemical content contained in the extract of *Catharanthus roseus* has been analyzed in several studies. The phytochemical results of *Catharanthus roseus* were summarized in Table 1.

**Table 1:Phytochemical Content from *Catharanthus roseus***

<b>Plant Parts</b>	<b>Content Compound</b>	<b>Type of Extract</b>	<b>Reference</b>
Leaves	Phenol	Rutin, quercetin and kaempferol	Ethanol extract
All parts of the plant	Alkaloids	Catharoseumine	Methanol extract
All parts of the plant	Alkaloids	Cathachunine	Ethanol extract
Leaves	Alkaloids	Vindoline	Water extract
Leaves	Alkaloids	Vindoline, vindolidine, vindolicine and vindolinine	Dichloromethane Extract
Leaves	Alkaloids	Vindogentianin, vindoline, vindolidine, vindolicine, vindolinine, perivine, and serpentine	Dichloromethane Extract
Leaves and twigs	Alkaloids	Vindoline, catharanthine and vinblastine	Water extract
Leaves and stems	Alkaloids, steroids, saponins, cardiac glycosides, cynogenic glycosides, flavonoids, phenols, phlobatannins		Water and methanol extract
Leaves	carbohydrates, proteins, amino acids, alkaloids, flavonoids, glycosides, tannins, steroids, phytosterols, phenols, saponins, and resins		Methanol extract

Based on the research of Rao *et al.*, the determination of phenolic compounds in the leaves of *Catharanthus roseus* can be carried out using the HPLC method using ethanol extraction. This study proved that the extract of *C.roseus* contained phenolic compounds, namely rutin, quercetin, and kaempferol. The amounts of rutin, quercetin, and kaempferol compounds in *C.roseus* were 21.59%, 0.12%, and 0.028% w/v, respectively<sup>14</sup>.

Wanget *al.* identified the type of alkaloid compound in *Catharanthus roseus* using column chromatography. All parts of the plant were extracted using ethanol. The results showed that *C.roseus* contains an alkaloid compound, Catharoseumine (22.0 mg)<sup>15</sup>.

Wanget *al.* also identified alkaloids in *C.roseus* using column chromatography. Whole plant parts of *C.roseus* were extracted with dichloromethane. The results showed that *C.roseus* contains an alkaloid compound, cathachunine (25.0 mg)<sup>16</sup>.

In another study, Gobozaet *al.* measured the concentrations of vindoline and selected phenolic compounds in aqueous, methanol, dichloromethane, and ethyl acetate extracts from the leaves of *Catharanthus roseus*. HPLC results showed that the methanol extract of *C.roseus* had the highest concentrations of chlorogenic acid (225.19 $\mu$ g/g), quercetin (1.945 $\mu$ g/g), coumarin (28.822 $\mu$ g/g), and rutin (85.916 $\mu$ g/g). At a wavelength of 220 nm, vindoline was dominant in the dichloromethane and ethyl acetate extracts with concentrations of 57,891 $\mu$ g/g and 57,323 $\mu$ g/g, respectively. The aqueous extract showed the lowest vindoline concentration (7,056 $\mu$ g/g) from *C.roseus*. It can be concluded that the leaves of *C.roseus* have vindoline compounds and were found to be dominant in the extracts of dichloromethane and ethyl acetate with concentrations of 57.891 $\mu$ g/g and 57,323 $\mu$ g/g, respectively<sup>17</sup>.

Tiong *et al.* identified alkaloid compounds from the dichloromethane extract of *Catharanthus roseus* using the Preparative Thin Layer Chromatography (TLC) method. This study reported the presence of vindoline (428.1 mg), vindolidine (57.9 mg), vindolicine (31.0 mg), and vindolinine (8.4 mg) compounds in *C. roseus* leaf extract with antidiabetic and antioxidant activity<sup>18</sup>.

Tiong *et al.* conducted a special study of its hypoglycemic activity and found vindogentianine, a new alkaloid, and six known alkaloids, vindolidine and vindolicine, vindolinine, perivine, and serpentine isolated from dichloromethane leaf extract of *Catharanthus roseus*. Tests using this preparative thin-layer chromatography method showed the presence of vindogentianine compounds (38.6 mg)<sup>19</sup>.

The alkaloid test on fresh leaves and twigs of *Catharanthus roseus* was carried out by Zhang *et al.* using aqueous extract. The total alkaloid content was determined colorimetrically with a bromophenol blue reagent. Preliminary phytochemical analysis showed that vindoline, catharanthine, and vinblastine content was  $14.76 \pm 0.74$ ,  $6.40 \pm 0.68$ , and  $2.83 \pm 0.16\%$ , respectively<sup>20</sup>.

Sudevan *et al.* evaluated metabolic compounds from aqueous and methanol extracts in *Catharanthus roseus* (leaves and stems). Qualitative phytochemical analysis was conducted to detect alkaloids, saponins, steroids, flavonoids, cardiac glycosides, cynogenic glycosides, and phlobatannins. The results showed that *C. roseus* extract contained alkaloids, saponins, steroids, flavonoids, cardiac glycosides, and cynogenic glycosides. Meanwhile, phlobatannins were not found in the methanol and water extracts of *C. roseus*. The active compounds were separated using the Thin Layer Chromatography (TLC) method and showed the presence of alkaloids, flavonoids, lipids, and terpenoids in this plant<sup>21</sup>.

The initial phytochemical screening conducted by Yamukujije *et al.* used methanol extract from the leaves of *Catharanthus roseus*. The results of phytochemical screening showed the presence of alkaloids, tannins, saponins, phytosterols, and carbohydrates in the leaf extract of *C. roseus*<sup>22</sup>.

### Antidiabetic Activity

Research on the antidiabetic activity of *Catharanthus roseus* extract has been carried out in several studies, both in vivo and in vitro. The result of the *Catharanthus roseus* antidiabetic study was summarized in Table 2.

**Table 2. Antidiabetic Activity of *Catharanthus roseus* (In Vivo and In Vitro Studies)**

Type of Extract	Plant Parts	Dose/Concentration	Methods	Parameter	Reported Activity	Reference
Water extract	Flowers, leaves, roots, and stems	250 mg/kg BW	Alloxan induction (75 mg/kg) in male Mus Musculus rats strain CD-1 (in vivo)	Blood glucose	The aqueous extract (250 mg/Kg) of the <i>C. roseus</i> plant has a significant hypoglycemic effect	<sup>23</sup>
Water extract	Leaves	10mg/100g BW	Alloxan induction (150 mg/kg) in albino rat wistar strain (in vivo)	Blood glucose	The results showed that the administration of water extract on alloxan-induced <i>C. roseus</i> leaves significantly reduced blood glucose levels	<sup>24</sup>
Methanol extract	Leaves	200 and 400 mg/kg BW	Streptozotocin induction for five days in male albino swiss rats (in vivo)	Serum glucose	Methanol extract from <i>C. roseus</i> leaves at a dose of 200 mg/kg body weight resulted in a significant decrease in serum glucose levels	<sup>12</sup>
Ethanol extract	Leaves	100 and 200 mg/kg BW	Streptozotocin induction (55 mg/kg) in male rats Wistar strain (in vivo)	Bodyweight and blood glucose	The results showed that the glucose transport gene level increased and returned to near normal values at a dose of 200 mg/kg <i>C. roseus</i> and there was no significant difference from the initial body weight of the mice.	<sup>7</sup>
Methanol extract	Leaves	250 mg/kg BW	Alloxan induction (110 mg/kg) in albino mice (In vivo)	Blood glucose	<i>C. roseus</i> methanol extract had a hypoglycemic effect, and the highest percentage of lowering blood glucose was shown by the extract+metformin combination at 72 hours (64.86%)	<sup>25</sup>
Ethanol extract	Leaves	400, 300 and 200 mg/kg BW	Alloxan induction in adult albino rats (150 mg/kg) (in vivo)	Blood glucose and body weight	Body weight and glucose-6-phosphate dehydrogenase are significantly increased and have an antioxidant effect	<sup>26</sup>
Ethanol extract	Leaves	300 mg/kg BW	Alloxan induction (150 mg/kg) in male albino rats wistar strain (in vivo)	Blood glucose, plasma insulin, plasma C-peptide, liver glycogen, total and glycosylated hemoglobin	Administration of ethanol extract from the stems of <i>C. fenzliratum</i> and leaves of <i>C. roseus</i> to alloxan-induced diabetic rats could restore the status of biochemical parameters to a near normal range.	<sup>27</sup>
Ethanol extract	Leaves	100 mg/kg BW	Streptozotocin induction (50 mg/kg) in albino rats wistar strain (in vivo)	Blood glucose and body weight	The results showed that the average weight of the mice was significantly increased. Meanwhile, on blood glucose levels, the administration of a mixture of 2 plants significantly reduced blood glucose levels	<sup>28</sup>

Type of Extract	Plant Parts	Dose/Concentration	Methods	Parameter	Reported Activity	Reference
Water extract	Leaves and twigs	50, 100 and 150 mg/kg BW	Streptozotocin induction (50 mg/kg) in male rats Wistar strain (in vivo)	Blood glucose and plasma insulin	At a 150 mg/kg dose of <i>C.roseus</i> , there was a more than 60% reduction in blood glucose and an almost 2.5-fold increase in plasma insulin and antioxidant effects.	20
Methanol extract	Leaves	250 mg/kg BW	Alloxan induction (120 mg/kg) in male albino rats (in vivo)	Blood glucose and serum protein	This study reports that <i>C.roseus</i> can lower blood glucose levels and restore serum protein to normal levels	29
Ethanol extract	Leaves	0.04, 0.08, 0.16 g/kg BW	Sucrose induction (3 g/kg) in white male rats Wistar strain (in vivo)	Blood glucose	<i>C.roseus</i> has the effect of lowering blood glucose levels in male white Wistar rats	30
Water extract	Leaves	1 and 2 g/kg BW	Sucrose induction (3 g/kg) in local male rabbits (in vivo)	Blood glucose and pancreatic insulin immunohistochemistry	A dose of 2 g/kg BW can reduce blood glucose levels in a state of hyperglycemia. Immunohistochemically it can be stated that the aqueous extract of <i>C.roseus</i> can stimulate pancreatic beta cells to produce the hormone insulin	31
Extracts of water, methanol, dichloromethane, and ethyl acetate	Leaves	a) 50, 25, 12.5, and 6.25 mg/mL for test inhibition of alpha-amylase and glucosidase b) vindoline (0.125 mM), CR-Meth (0.0625 mg/mL), CR-DCM (0.0625 mg/mL) and CR-Aq (0.3125 mg/mL) for insulin secretion test	Pancreatic RIN-5F cells in mice (in vitro)	Insulin secretion, alpha-amylase, and glucosidase inhibition	Alpha-glucosidase inhibitory activity was significant in all plant extracts at 50 mg/mL. Inhibitory activity of alpha-amylase methanol extract showed inhibition of about 40% with a dose of 50 mg/mL. In RIN-5F cells previously exposed to 50 mM glucose, vindoline (0.125 mM) markedly increased insulin secretion	17

### ***In Vivo Studies***

Based on research by Vega-Ávila *et al.*, antidiabetic activity can be determined using aqueous extracts on the roots, leaves, flowers, and stems of *Catharanthus roseus*. This extract's blood-glucose-lowering activity was determined in healthy and alloxan-induced diabetic rats (75 mg/Kg) after intraperitoneal administration (250 mg/Kg body weight). The animal group consisted of 6 rats. It consisted of 3 healthy rats and three diabetic rats. Blood samples were taken, and blood glucose was used as a parameter. It was proven that aqueous extract (250 mg/Kg) from flowers, leaves, roots, and stems of *C.roseus* significantly produced a hypoglycemic effect in healthy and diabetic mice given alloxan. The aqueous extract of the leaves had the best hypoglycemic effect in healthy rats. Meanwhile, the best hypoglycemic effect in diabetic rats was seen in the aqueous extract of the stems<sup>23</sup>.

Muralidharan conducted a study on the leaves of *Catharanthus roseus* by intraperitoneal administration of a single dose of 10 mg/100 g every morning for 30 days. The number of rats used in this study was 32, divided into 16 live diabetic and 16 control rats. Mice were further divided into four groups of 8 each: control (C), control mice given *C.roseus* (C+CR), diabetes (D), and diabetic animals treated with *C.roseus* (D+CR). Diabetes in rats was given by administering alloxan intraperitoneally at 150 mg/kg body weight. Blood glucose level was used as a parameter. The results showed that administration of aqueous extract on alloxan-induced *C.roseus* leaves significantly reduced blood glucose levels<sup>24</sup>.

Research by Singh *et al.* used male Swiss albino mice as experimental animals. Mice were divided into diabetic (D) and non-diabetic (ND) groups, with five mice in each group. Diabetes was induced by intraperitoneal administration of streptozotocin for five consecutive days. Meanwhile, the methanol extract of *C.roseus* leaves at a dose of 200 and 400 mg/kg body weight was induced intraperitoneally in mice. Serum glucose level is used as the parameter. This study has shown that the methanol extract of *C.roseus* leaves at a dose of 200 mg/kg body weight resulted in a significant reduction in serum glucose levels<sup>12</sup>.

Al-Saqha *et al.* experimented on 30 male Wistar rats divided into five groups, where each group consisted of 6 rats. Group 1: standard control, group 2: diabetes control, groups 3 and 4: diabetic rats treated with ethanol extract of *Catharanthus roseus* leaves at doses of 100 and 200 mg/kg, and group 5: diabetic rats given metformin 100 mg/kg. Diabetes was induced in rats by intraperitoneal injection of streptozotocin 55 mg/kg body weight. The parameters used were body weight and blood glucose. The results showed that *C.roseus* at a dose of 200 mg/kg was more effective in reducing fasting blood glucose levels, and there was no significant difference in the initial body weight of rats<sup>7</sup>.

Research by Ohadoma *et al.* investigated the effect of *Catharanthus roseus* methanol leaf extract on hypoglycemic activity compared to metformin and glibenclamide in rats. Rats were divided into six groups, where each group consisted of 5 rats. Groups 2, 3, and 4 received 250 mg/kg of *C.roseus* extract, 100 mg/kg of metformin, and 1 mg/kg of glibenclamide, respectively. Meanwhile, groups 5 and 6 were given a combination of metformin extract and glibenclamide extract, respectively, at the above doses. Group 1 was the control and only received distilled water. Diabetic rats had alloxan injected intraperitoneally at 110 mg/kg. Blood glucose was used as a parameter. The results obtained in this study showed that the methanolic extract of *C.roseus* had a hypoglycemic effect and the highest percentage of lowering blood glucose as indicated by the combination of extract+metformin at 72 hours (64.86%)<sup>25</sup>.

The antidiabetic study by Muralidharan used 32 male rats (Albino, Wistar) as experimental animals. Rats were divided into four groups, each consisting of 8 rats. Divided over control (C); control mice given C.

*roseus* (C+CR); diabetes (D); and diabetic animals treated with *C.roseus*(D+CR). The ethanol extract from the leaves of *Catharanthus roseus* was given at doses of 400, 300, and 200 mg/kg body weight of rats. The control group was given phosphate-buffered saline orally for 21 days. Diabetic rats were given alloxan 150 mg/kg body weight intraperitoneally. Bodyweight and blood glucose were determined and used as parameters. The results obtained from this study showed that the effect of *C.roseus* leaf extract on animal body weight increased significantly ( $p>0.05$ ) compared to controls and was influential in controlling elevated blood glucose levels<sup>26</sup>.

Manoharan et al. proved the antihyperglycemic effect of *Catharanthus roseus* and *Cosmocarpus fenerstratum* in alloxan-induced diabetic rats. A total of 42 rats were divided into seven groups, and each group containing six rats was used as experimental animals. Rats were induced with alloxan (150 mg/kg BW) intraperitoneally to make rats diabetic. The antidiabetic potential of this plant was evaluated by analyzing the status of blood glucose, plasma insulin, plasma C-peptide, liver glycogen, and total and glycosylated hemoglobin as parameters. The results showed that administration of ethanol extract from the stems of *C. fenerstratum* and leaves of *C.roseus* to alloxan-induced diabetic rats could restore the status of biochemical parameters to a near normal range. This study concluded that the ethanolic extract of the leaves of *C.roseus* (300 mg/kg BW) had a strong antihyperglycemic effect in alloxan-induced diabetic rats<sup>27</sup>.

Rajashree et al. also studied the hypoglycemic effect of a mixture of 2 plants, namely extracts of *Salacia reticulata* and *Catharanthus roseus*, evaluated in streptozotocin-induced rats. Wistar strain albino rats were divided into four groups, each group consisting of 6 rats. Group 1: normal control mice. Group 2: diabetic control rats. Group 3: diabetic rats injected with insulin. Group 4: diabetic rats treated orally with a mixture of *S. reticulata* and *C.roseus*, each 100 mg/kg body weight/day. Diabetic rats were induced by streptozotocin 50 mg/kg BW intraperitoneally. The animal body weight and blood glucose levels were observed and set as parameters. The results showed that the mean weight of the rats fed the formula significantly increased compared to the diabetic controls. Meanwhile, on blood glucose levels, the administration of the mixed formula significantly reduced blood glucose levels compared to diabetes control and insulin-treated diabetic rats. This study proves that the ethanolic extract of *C.roseus* (100 mg/kg body weight) in diabetic rats can reduce blood glucose levels to close to control levels<sup>28</sup>.

Zhang et al. conducted a study on the antihyperglycemic and antioxidant effects of the aqueous extract of the leaves and twigs of *Catharanthus roseus*. This experiment used 36 male Wistar rats (30 diabetic and six normal rats). Determination of blood glucose and plasma insulin levels were performed as parameters. At a 150 mg/kg dose of *C.roseus*, there was a more than 60% reduction in blood glucose and an almost 2.5-fold increase in plasma insulin in streptozotocin-treated animals. This study shows that *C.roseus* significantly lowers blood glucose levels and increases insulin levels<sup>20</sup>.

Fresh leaves of *Catharanthus roseus* were extracted with methanol in the research of Aruljithi et al. The experimental animal used was a male albino rat. Animals were divided into four groups, each group containing four rats. Group 1: rats were kept as controls. Group 2: induced alloxan (120 mg/kg body weight). Group 3: induced alloxan (120 mg/kg body weight) + *C.roseus* as treatment (250 mg/kg body weight). Group 4: induced alloxan (120 mg/kg BW) + insulin (5 mg/kg BW). Blood glucose and serum protein levels were used as parameters. This study reports that *C.roseus* can lower blood glucose levels and restore serum protein to normal levels<sup>29</sup>.

The test animals used in Soriton et al. study were 15 white male rats of the Wistar strain, divided into five groups. Before being given treatment, all rats were induced by a sucrose solution of 5,625 g/Kg BW. Parameter data was obtained from the examination of blood glucose levels. Based on the measurement results, the ethanolic extract of the leaves of *Catharanthus roseus* with doses of 0.04, 0.08, and 0.16 g/kg BW had the effect of lowering blood glucose levels in Wistar male white rats<sup>30</sup>.

In the study of Widyastuti et al., 15 local male rabbits were used. Then the rabbits were grouped into five treatment groups, each consisting of 3 rabbits. Rabbits were given sucrose 3 g/kg BW orally to induce hyperglycemia. The parameters for this study were analyzing blood glucose levels and detecting insulin in the pancreas by immunohistochemistry. The results showed that the administration of *Catharanthus roseus* leaf water extract at a dose of 1 g/kg BW had not been able to reduce blood glucose levels. In comparison, administering a dose of 2 g/kg BW reduced blood glucose levels in hyperglycemic rabbits and was not significantly different compared with glibenclamide drug treatment. Immunohistochemically, it can be stated that the aqueous extract of *C.roseus* can stimulate pancreatic beta cells to produce the hormone insulin<sup>31</sup>.

### ***In Vitro Studies***

Research conducted by Goboza et al. is an in vitro test on *Catharanthus roseus* leaves using various extracts. The extracts were water extract, methanol, dichloromethane, and ethyl acetate. Insulin secretion, alpha-amylase, and glucosidase inhibition were used as parameters. The results showed that the alpha-glucosidase inhibitory activity was quite large in all plant extracts at 50 mg/mL. The inhibitory activity of alpha-amylase methanol extract showed much higher inhibition of about 40% at a 50 mg/ml dose. In RIN-5F cells previously

exposed to 50 mM glucose, vindoline (0.125 mM) markedly increased insulin secretion (0.72 ng/mL). Based on the results obtained in this study, *C.roseus* can be used in pharmaceutical applications, especially in managing diabetes<sup>17</sup>.

#### **IV. Discussion**

*Catharanthus roseus* is a valuable plant for treating diabetes as an alternative to chemical drugs. This plant contains various phytochemical compounds that can lower blood glucose levels in every part of the plant. The main compound in *C.roseus* is vindoline which is an alkaloid group. Alkaloids are known to play a role in lowering blood glucose levels by stimulating the hypothalamus to increase the secretion of Growth Hormone Releasing Hormone (GHRH) so that the secretion of Growth Hormone (GH) in the pituitary increases. High GH levels will stimulate the liver to secrete Insulin-like Growth Factor-1 (IGF-1). IGF-1 has the effect of lowering blood sugar levels and reducing gluconeogenesis<sup>32</sup>. Several studies have also shown that the alkaloids contained in *C.roseus* can lower blood glucose and increase insulin levels<sup>20 17 18</sup>. Then on histopathological observations, alkaloids showed the presence of repair of damaged pancreatic tissue. This can increase the amount of insulin in the body. Then blood glucose will enter the cells to decrease blood glucose in the body<sup>33</sup>.

#### **V. Conclusion**

*Catharanthus roseus* plant has many benefits among the community as traditional medicine. Studies on the chemical components of *C.roseus* have been shown to contain many active substances in all parts of the plant, such as alkaloids, phenols, steroids, saponins, cardiac glycosides, cyanogenic glycosides, flavonoids, phlobatannins, carbohydrates, proteins, amino acids, tannins, phytosterols, and resins were the main compounds of *C.roseus* namely vindoline which is an alkaloid group. Judging from its many active substances, *C.roseus* has many benefits for the body, one of which is antidiabetic.

Through studies in vivo and in vitro, *C.roseus* is reported to have the ability to lower blood glucose and increase insulin levels. This confirms that *C.roseus* has potential as an antidiabetic. However, further research needs to be done to ascertain its antidiabetic activity in the future by understanding metabolism in the body and receptor interactions associated with diabetes. Further study of activities *C.roseus* must provide clear sources of specifications for the ingredients used, mainly when plant extracts are used.

#### **References**

- [1]. American Diabetes Association. *Diagnosis and Classification of Diabetes Mellitus*. Vol 37.; 2014. doi:10.2337/dc14-S081
- [2]. PERKENI. *Pedoman Pengelolaan Dan Pencegahan Diabetes Melitus Tipe 2 Di Indonesia* 2021. PB PERKENI; 2021.
- [3]. *International Diabetes Federation*. 10th ed.; 2021. www.diabetesatlas.org
- [4]. Putra RJS, Anisyah A, P HR. Kejadian Efek Samping Potensial Terapi Obat Anti Diabetes Pada Pasien Diabetes Melitus Berdasarkan Algoritme Naranjo. *Pharm J Indones*. 2017;2(2):45-50.
- [5]. Pandanwangi S, Zuniarto AA, Mubarok H. Analisa Drug Related Problems (Drps) Pasien Gagal Ginjal Dengan Komplikasi Diabetes Mellitus di RSUD X. *Pharma Xplore J Ilmu Farm*. 2018;3(1):170-183.
- [6]. Mishra JN, Verma NK. A brief study on Catharanthus Roseus: A review Jai. *Int J Res Pharm Pharm Sci*. 2017;2(2):20-23.
- [7]. Al-Shaqha WM, Khan M, Salam N, Azzi A, Chaudhary AA. Antidiabetic potential of Catharanthus roseus Linn. and its effect on the glucose transport gene (GLUT-2 and GLUT-4) in streptozotocin-induced diabetic Wistar rats. *BMC Complement Altern Med*. 2015;15(379):1-8. doi:10.1186/s12906-015-0899-6
- [8]. Keerthana S, Mahalakshmi S, Kavitha S, Ramesh BN., Sivaraj C, Arumugam P. Antioxidant and Anticancer Activities of Roots of Catharanthus roseus (L.) G.Don. *Res J Chem Environ*. 2021;25(4):158-165.
- [9]. Govindasamy C, Srinivasan R. In vitro antibacterial activity and phytochemical analysis of Catharanthus roseus (Linn.) G. Don. *Asian Pac J Trop Biomed*. Published online 2012:155-158.
- [10]. Alam MM, Naeem M, Khan MMA, Uddin M. *Vincristine and Vinblastine Anticancer Catharanthus Alkaloids: Pharmacological Applications and Strategies for Yield Improvement*; 2017. DOI 10.1007/978-3-319-51620-2\_11
- [11]. Sayed M., Jesmin Ms., Sarker T., Rahman M., Alam M. Antitumor Activity of Leaf Extracts of Catharanthus roseus (L.) G. Don. *Plant Environ Dev*. 2014;3(2):24-30.
- [12]. Singh A, Singh PK, Singh RK. Antidiabetic and Wound Healing Activity of Catharanthus roseus L. in Streptozotocin-Induced Diabetic Mice. *Am J Phytomedicine Clin Ther*. 2014;2(6):686-692.
- [13]. Aboelnaga SMH. Evaluation of the Antihyperlipidemic and Antioxidant Effects of Catharanthus roseus Extracted from Vinca minor in Diabetic Rats. *J Pharm Res Int*. 2021;33(2):1-13.

doi:10.9734/jpri/2021/v33i231142

- [14]. Rao SA, Ahmed MF. Simultaneous Determination of Phenolic Compounds in Catharanthus roseus Leaves by HPLC method. *Int J Pharm Sci Res.* 2014;5(3):976-981. doi:10.13040/IJPSR.0975-8232.5(3).976-81
- [15]. Wang L, He H-P, Di Y-T, Zhang Y, Hao X-J. Catharoseumine, a new monoterpenoid indole alkaloid possessing a peroxy bridge from Catharanthus roseus. *Tetrahedron Lett.* 2012;53(53):1576-1578. doi:10.1016/j.tetlet.2012.01.060
- [16]. Wang X-D, Li C-Y, Jiang M-M, et al. Induction of apoptosis in human leukemia cells through an intrinsic pathway by cathachunine, a unique alkaloid isolated from Catharanthus roseus. *Phytomedicine.* 2016;23:641-653. doi:10.1016/j.phymed.2016.03.003
- [17]. Goboza M, Meyer M, Aboua YG, Oguntibeju OO. In vitro antidiabetic and antioxidant effects of different extracts of Catharanthus roseus and its indole alkaloid, vindoline. *Molecules.* 2020;25(5546):1-22. doi:10.3390/molecules25235546
- [18]. Tiong SH, Looi CY, Hazni H, et al. Antidiabetic and antioxidant properties of alkaloids from Catharanthus roseus (L.) G. Don. *Molecules.* 2013;18:9770-9784. doi:10.3390/molecules18089770
- [19]. Tiong SH, Looi CY, Arya A, et al. Vindogentianine, a hypoglycemic alkaloid from Catharanthus roseus (L.) G. Don (Apocynaceae). *Fitoterapia.* 2015;102:182-188. doi:10.1016/j.fitote.2015.01.019
- [20]. Zhang L, Wei G, Liu Y, Zu Y, Gai Q, Yang L. Antihyperglycemic and antioxidant activities of total alkaloids from Catharanthus roseus in streptozotocin-induced diabetic rats. *J For Res.* 2016;27(1):167-174. doi:10.1007/s11676-015-0112-2
- [21]. Sudevan S, Paramasivam R, Sundar S, R, Awathy A R RR, Vijayarghavan R. Evaluation of Metabolic Compounds of Catharanthus Roseus and Its Anticancer Activity. *Eur J Pharm Med Res.* 2017;4(9):282-290.
- [22]. Yamukujije C, Ndacyayisenga J. Phytochemical Analysis & In Vitro Anticancer Activity of Methanol Extract of Catharanthus Roseus Leaves Using HEPG2 Cell Line. *IAETSD J Adv Res Appl Sci.* 2019;6(8):10-17.
- [23]. Vega-Ávila E, Cano-Velasco JL, Alarcón-Aguilar FJ, Fajardo Ortiz MDC, Almanza-Pérez JC, Román-Ramos R. Hypoglycemic activity of aqueous extracts from catharanthus roseus. *Evidence-based Complement Altern Med.* Published online 2012:7. doi:10.1155/2012/934258
- [24]. Muralidharan L. Catharanthus roseus Leaves as an Antidiabetic and Hypolipidemic Agents in Alloxan - Induced Diabetic Rats. *Am J Phytomedicine Clin Ther.* 2014;2(12):1393-1396.
- [25]. Ohadoma S, Michael H. Effects of co-administration of methanol leaf extract of Catharanthus roseus on the hypoglycemic activity of metformin and glibenclamide in rats. *Asian Pac J Trop Med.* Published online 2011;475-477.
- [26]. Muralidharan L. Hypoglycemic and Biochemical Remedies Of Catharanthus Roseus (Linn) on Alloxan-Induced Diabetic Rat and Its Anti Oxidant Status in Rat Lenses. *Int J Med Res Pharm Sci.* 2015;2(1):1-6.
- [27]. Manoharan S, Umadevi S, Jayanthi S, Baskaran N. Antihyperglycemic effect of Coscinium fenestratum and Catharanthus roseus in alloxan-induced diabetic rats. *Int J Nutr Pharmacol Neurol Dis.* 2011;1(2):189-193. doi:10.4103/2231-0738.84213
- [28]. Rajashree R, Bhat PP, Ravishankar M V. Effects of a Mixture Of Salacia reticulata W. and Catharanthus roseus L. Extracts in Streptozotocin-Induced Juvenile Diabetic Rats. *J Physiol Biomed Sci.* 2011;24(1):5-8.
- [29]. Aruljothi B, Samipillai SS. Antidiabetic activity of Catharanthus roseus in alloxan-induced diabetics rats. *Int J Mod Res Rev.* 2016;4(3):1121-1124. www.journalijmrr.com
- [30]. Soriton H, Yamlean PVY, Lolo WA. Uji Efektivitas Ekstrak Etanol Daun Tapak Dara (Catharanthus roseus (L.) G.Don) terhadap Penurunan Kadar Gula Darah Tikus Putih Jantan Galur Wistar (Rattus norvegicus L.) yang diinduksi Sukrosa. *Pharmacon.* 2014;3(3):162-169.
- [31]. Widyastuti S, Suarsana IN. Ekstrak Air Tapak Dara Menurunkan Kadar Gula dan Meningkatkan Jumlah Sel Beta Pankreas Kelinci Hiperglikemia. *J Vet.* 2011;12(1):7-12.
- [32]. Wulandari. Uji Efektivitas Antihiperglikemia Kombinasi Jus Pare (Momordica charantia L) dan Jus Tomat (Solanum lycopersicum L) pada Tikus Wistar Jantan dengan Metode Toleransi Glukosa. *Pharm Sci Res.* 2016;3(3):145-154.
- [33]. Prameswari OM, Widjanarko SB. Uji Efek Ekstrak Air Daun Pandan Wangi terhadap Penurunan Kadar Glukosa Darah dan Histopatologi Tikus Diabetes Mellitus. *J Pangan dan Agroindustri.* 2014;2(2):16-27.