

Vinca (*Catharanthus roseus*) containing phytochemicals and pharmacological profile

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Abstract

Catharanthus roseus (Vinca plant) is an important plant having many medicinal uses. It is popularly known as Madagascar periwinkle. It is small in size perennial herbaceous evergreen plant that was native to the Madagascar island. It has attracted increasing attention due to it being shown to possess a range of phytochemicals with various biological activities such as antioxidant, antibacterial, antifungal, antidiabetic and anticancer properties. It delivers about 130 alkaloids predominantly ajmalicine, vinceine, reserpine, vincristine, vinblastine and raubasine. Remarkably, vinblastine and vincristine isolated from this plant were the first plant-derived anticancer agents deployed for clinical use. This paper provides an overview of the traditional use and phytochemical profiles of *C. roseus*, and summarises updated techniques of the preparation of dried material, extraction and isolation of bioactive compounds from this plant. In addition, purported health benefits of the extracts and bioactive compounds derived from this plant were also addressed to support their potential as therapeutic agents.

Keywords: *Catharanthus roseus*; Bioactive compounds; Phytochemicals; Alkaloids; Health benefits

1 Introduction

Vinca is a genus of flowering plants in the family Apocynaceae, native to Europe, northwest Africa and southwest Asia. The English name periwinkle is shared with the related genus *Catharanthus* (and also with the common seashore mollusc, *Littorina littorea*).^{[1][2][3][4][5]} Amongst the plethora of medicinal plants identified, *Catharanthus roseus* (L.) G. Don (*C. roseus*) has been widely used to treat various diseases in many countries. The hot water extract of the dried *C. roseus* leaf has been used for the treatment of diabetes in Jamaica, Kenya and the West Indies or the hot water extract of the dried plant has been taken orally as complementary and alternative therapies for various types of cancers, heart disease and leishmaniasis in Peru.^[6] The flowers produced by these plants are planted for decorative purposes are of colours such as pink, purple and white. Madagascar periwinkle is used traditionally for number of ailments such as high blood pressure, infection and diabetes mellitus. Stem produces a milky sap which is a source for more than 70 indole alkaloids. Vincristine and vinblastine were isolated from this plant are well known anti-cancer drugs for Hodgkin's lymphoma and childhood leukemia respectively.

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Figure 1 The flowers of *Catharanthus roseus* G. Don. *Catharanthus roseus* (syn. *Vinca rosea*) an evergreen shrub, it grows to a height of 1 m with a spread of 1 m. The stem is short, erect and branching; the leaves are glossy green, oval, 5 cm long and opposite acuminate; the flowers are soft pink, tinged with red, 5 petal, open, tubular and 4 cm across, appearing in spring and autumn (three colors: pink, purple and white)

2 Scientific classification [7]

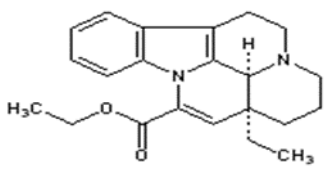
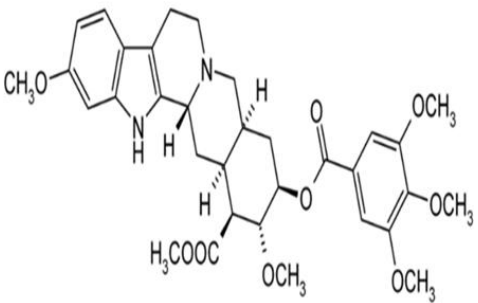
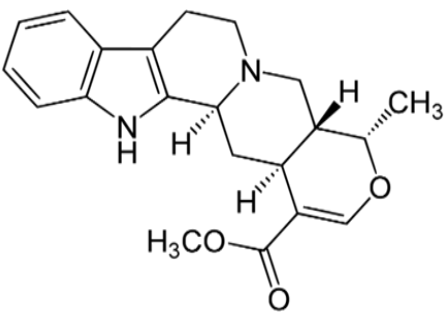
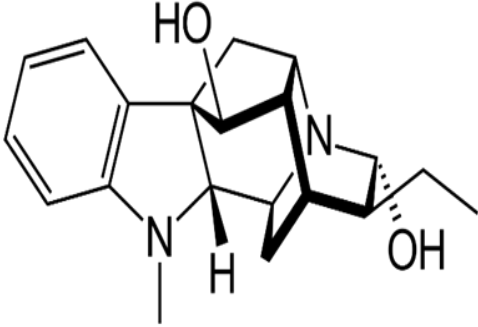
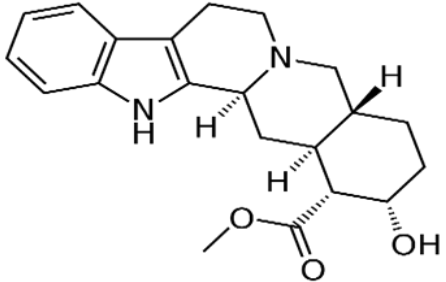
Botanical Name(s) :	<i>Vinca Rosea (Catharanthus roseus)</i>
Family Name:	Apocynaceae
Kingdom:	Plantae
Division:	Magnoliophyta (Flowering plants)
Class:	Magnoliopsida (Dicotyledons)
Order:	Gentianales
Family:	Apocynaceae
Genus:	<i>Catharanthus</i>
Species:	<i>C. roseus</i>

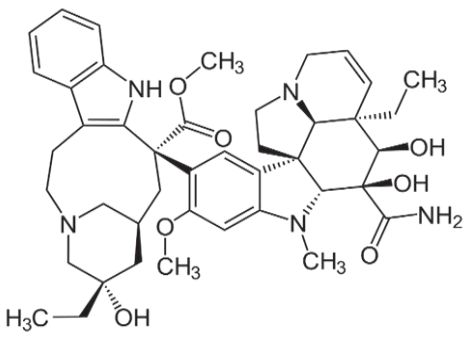
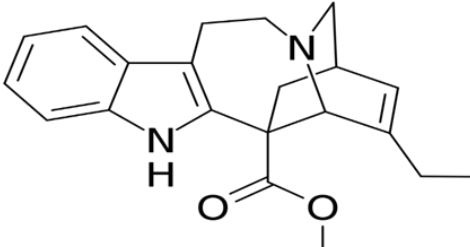
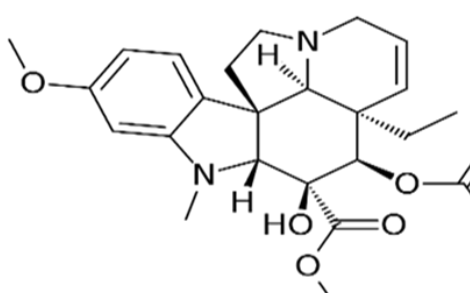
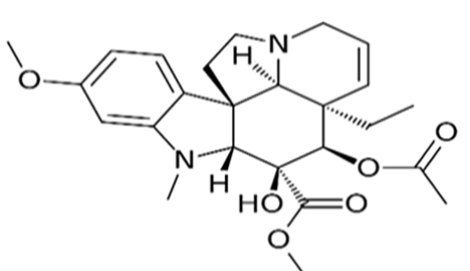
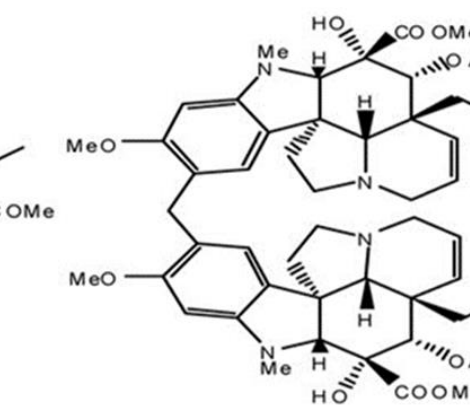
3 Major Bioactive Compounds Derived from *C. roseus*

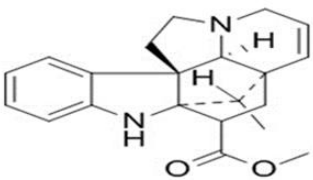
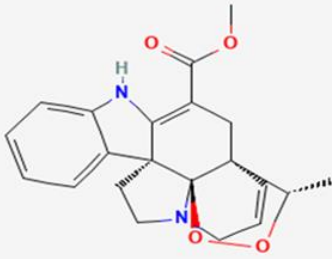
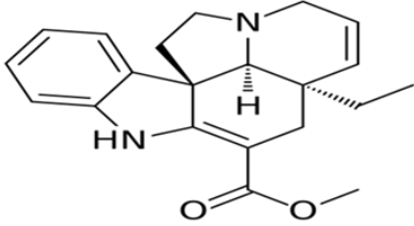
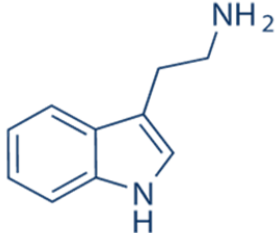
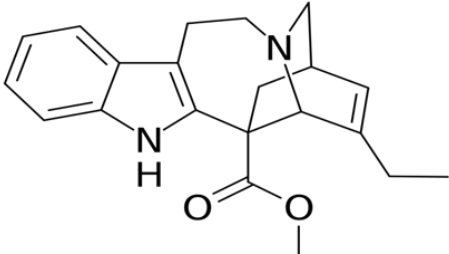
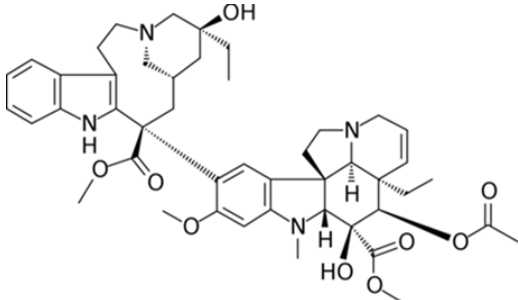
A range of alkaloids (nitrogen-containing organic compounds other than amino acids, peptides, purines and derivatives, amino sugars and antibiotics) [8] have been found in *C. roseus*. This plant has been found to possess a number of important bioactive components that greatly contribute to the herbal medicine industry; however, their amounts present in the plant are often low.

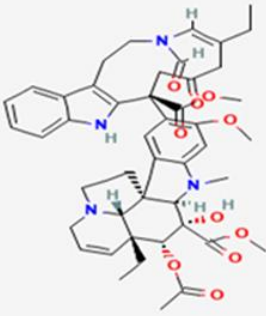
Table 1 Identified alkaloids in *C. roseus*

Alkaloids	Plant part	Quantity	Chemical structure
Vincristine	Leaf	0.189–0.523 mg/g DE	
	Stem	0.082–0.388 mg/g DE	
	Root	0.078–0.659 mg/g DE	
Vinblastine	Leaf	0.266–1.293 mg/g DE	
	Stem	0.285–1.056 mg/g DE	
	Root	0.463–1.638 mg/g DE	

Vinpocetine	Leaf	0.001–0.006 mg/g DE	
	Stem	0.001–0.007 mg/g DE	
	Root	0.001–0.056 mg/g DE	
Reserpine	Leaf	0.001–0.036 mg/g DE	
	Stem	0.003–0.055 mg/g DE	
	Root	0.001–0.036 mg/g DE	
Ajmalicine	Leaf	0.165–0.970 mg/g DE	
	Stem	0.162–5.487 mg/g DE	
	Root	0.124–17.675 mg/ DE	
Ajmaline	Leaf	0.016–0.067 mg/g DE	
	Stem	0.025–0.085 mg/g DE	
	Root	0,036–0.140 mg/g DE	
Yohimbine	Leaf	0.139–0.539 mg/g DE	
	Stem	0.185–1.572 mg/g DE	
	Root	0.316–2.433 mg/g DE	
Vindesine	Leaf	0.139–2.978 mg/g DE	
	Stem	1.754– 2.302 mg/g DE	

	Root	1.552–3.247 mg/g DE	
Catharanthine	Leaf	0.2843 +/- 0.0132 mg/g	
Vindolidine	Leaf	0.14 %	
Vindoline	Leaf	5.301-19.463 mg/g DE	
	Stem	0.144-3.344 mg/g DE	
	Root	0.021-9.690 mg/g DE	
Vindolicine	Leaf	0.07%	 III Vindolicine

Vindolinine	Leaf	0.02%	
Catharoseumine	Whole plant	0.786 mg/kg	
Tabersonine	Hairy root	NR	
Tryptamine	Hairy root	NR	
Catharanthamine	Leaf	NR	
14',15'-didehydrocyclovi nblastine	Whole plant	0.071 mg/g DE	

Catharine	Whole plant	0.098 mg/g DE	
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DE – Dry Extract , NR – Not Reported

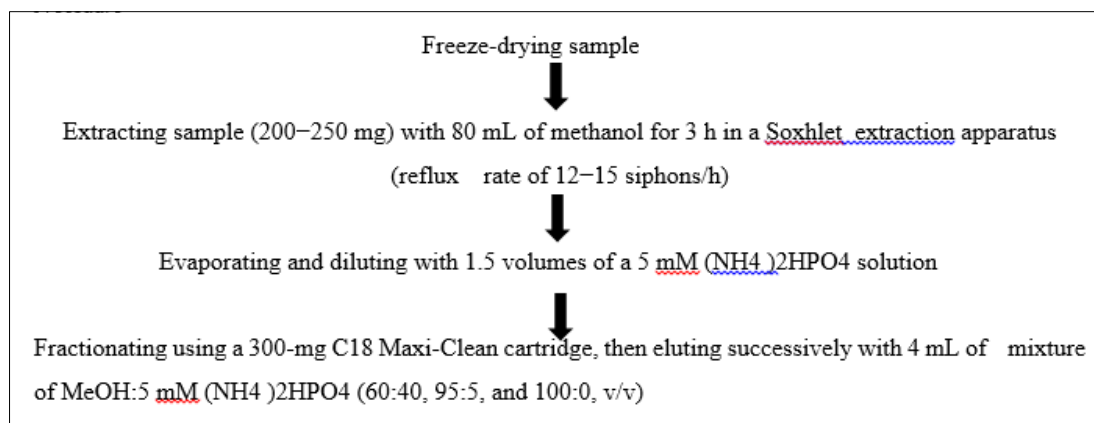
4 Preparation and Recovery of Bioactive Compounds from *C. roseus*

In previous studies, various drying methods, such as freeze drying, air drying, low-temperature drying, infrared drying or drying under the shade have been applied to prepare dried *C. roseus* for further recovery of bioactive compounds. The results showed that drying methods significantly affected the retention of bioactive compounds in *C. roseus* material because bioactive compounds are sensitive to heat, light and oxygen^[9]. Freeze drying has been reported as a prominent and effective drying method in terms of the retention of bioactive compounds, but it is costly and not typically available in some of the regions where the plant is collected and processed^[10]. Among thermal drying methods, infrared drying at 35 °C was found to be suitable for saponin retention within the *C. roseus* stem and root, while vacuum drying at 50 °C was suggested for drying the leaf and the flower, which contained high levels of phenolics and flavonoids^[9].

4.1 Plant part: Hairy root

Compounds: Vindoline, ajmalicine, serpentine, and catharanthine

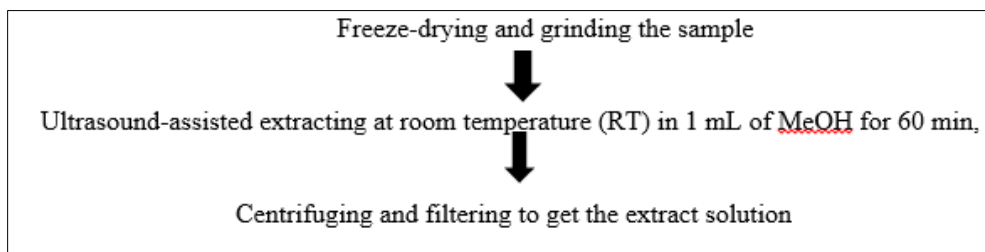
Procedure



4.2 Plant part: Hairy root

Compounds: Serpentine, vincristine, vindoline, catharanthine, vinblastine, tabersonine, tryptamine and ajmalicine

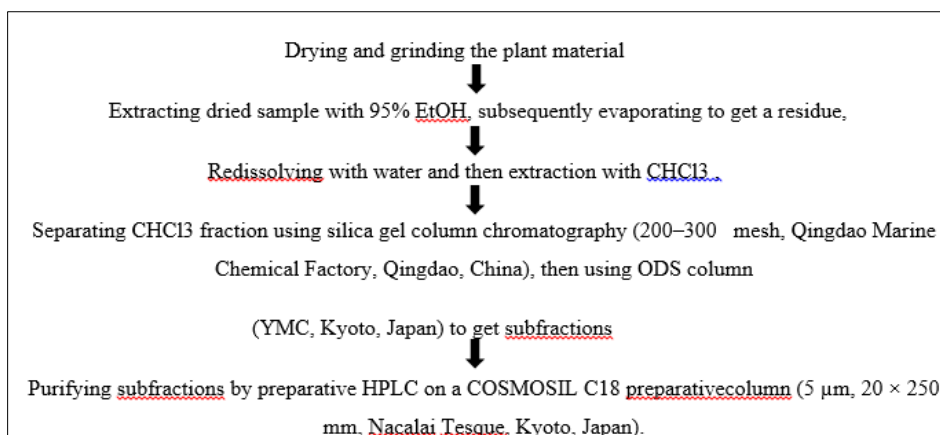
Procedure



4.3 Plant part: Whole plant

Compounds:- 140, 150 -didehydrocyclovinblastine, 17-deacetyoxycyclovinblastine, 17-deacetyoxivinamidine, vinamidin, leurosine, catharine, cycloleurosinez leurosidine and cathachunine

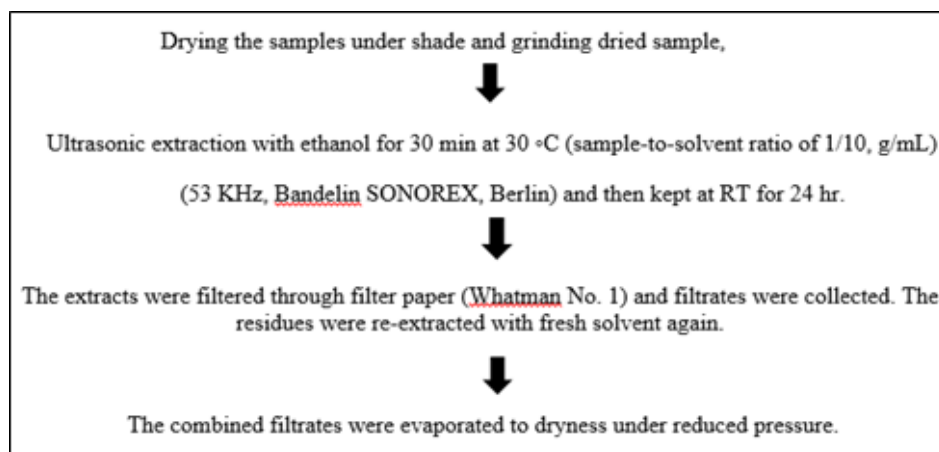
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4.4 Plant part :- Leaf, stem and root

Compounds:- Ajmaline, yohimbine, vindesine, ajmalicine, serpentine, vincristine, vinblastine, vindoline, vincopetine and reserpine

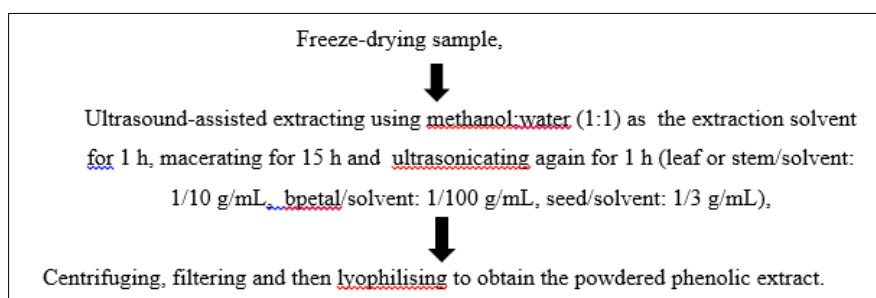
Procedure



4.5 Plant part: Leaf, stem, seed and petal

Compounds:- Caffeoylquinic acids, quercetin, kaempferol, isorhamnetin and their derivatives

Procedure



5 Pharmacological activity

5.1 Anti-cancer activity

C. roseus has been found to contain a range of alkaloids possessing anticancer activity including vinblastine, vincristine, vindoline, vindolidine, vindolicine, vindolinine and vindogentianine [11,12,13]. They inhibit cell proliferation through changing the microtubular dynamics, which induces apoptosis [14].

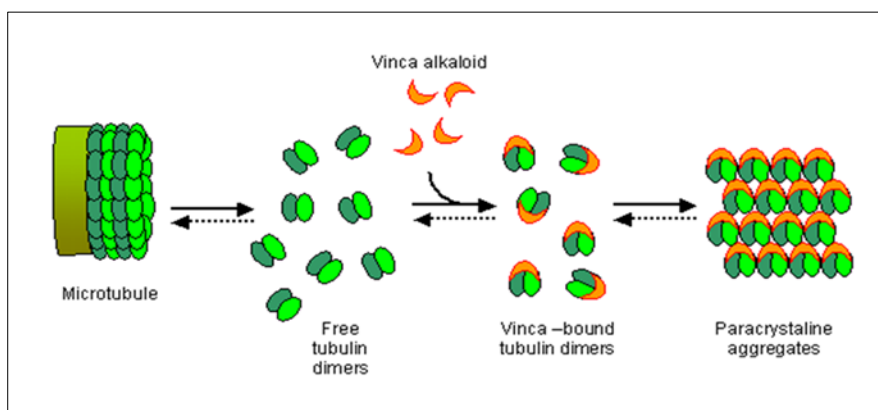


Figure 2 Mechanism of action of vincristine and vinblastine

5.2 Anti-diabetic activity

Vinca rosea of flowers and leaves have ethanolic extracts which is similar to the standard drug glibenclamide which is a hypoglycemic agent^[15,16,17]. Juice from the leaf of *C. roseus* was reported to produce a dose-dependent reduction in blood glucose of both normal and diabetic rabbits^[18]. The whole plant *C. roseus* methanolic extract displayed effective antihyperglycaemic activity, correlating with improvement in body weight, lipid profile and regeneration of β -cells of the pancreas in diabetic rats^[19].

5.3 Anti-microbial activity

Crude extracts from different parts of the plant show anti-bacterial activity against microorganism like *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Staphylococcus aureus*. The extracts could be used as the prophylactic agent in the treatment of many bacterial diseases^[20]

5.4 Wound healing property

The wound healing property was carried out using 100 mg / kg/day of *C. roseus* ethanol extract in rats. High rate of wound contraction was observed which significant decrease in epithelization period, marked increase in dry weight and hydroxyproline content of the granulation tissue as compared with the controls. Wound contraction together with increased tensile strength and hydroxyproline content provides evidence to the use of *C. roseus* in the management of wound healing^[21].

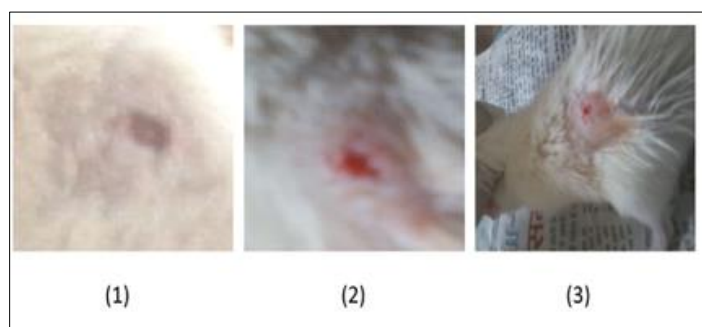


Figure 3 Photograph showing various stages of wound healing activity

5.5 Hypotensive activity

Extract obtained from the leaves of the *C. roseus* plant made significant change in hypotensive property. Remarkable antihyperglycemic and hypotensive activity of the leaf extracts (hydroalcoholic or dichloromethane-methanol) have been outlined in laboratory animals [22].

5.6 Anti-Ulcer Property

There are two alkaloids which have anti-ulcer property such as Vincamine and Vindoline . Vincamine has activity of cerebrovasodilatory and neuroprotective by the plant leaves but they induced gastric damage in rats [23].

5.7 Enhancement of memory

There is one alkaloid named Vinoceptine which has property to improve brain function and memory which is beneficial to Alzheimer's disease. Vinpocetine when subjected to a well-tolerated dose up to 60 mg/d in clinical trials of dementia and stroke proved no significant adverse events [24].

5.8 Alzheimer's disease

Vinpocetine has been reported to have a variety of actions to improve brain function and memory, particularly beneficial in the case of Alzheimer's disease. Vinpocetine when subjected to a well-tolerated dose up to 60 mg/d in clinical trials of dementia and stroke proved no significant adverse events [23].

5.9 Hypolipidemic activity

The leaf juice of *C. roseus* proved Significant anti atherosclerotic as observed by decline in the serum levels of total cholesterol, triglycerides, LDL-c, VLDL c as well as the histology of aorta, liver and kidney [24].

5.10 Anti-oxidant property

Anti -oxidant property is mainly found in the roots of pink and white flowers which have ethanolic extracts which is obtained from different assays such as hydroxyl radical-scavenging activity, superoxide radical-scavenging activity, DPPH radical-scavenging and nitric oxide radical inhibition method [22].

5.11 Anti-diarrheal property

Anti-diarrheal property is tested in wistar rats by the ethanolic leaf extracts and castor oil as an experiment of diarrhoea has pretreatment extract. The effect of anti-diarrheal was shown by the dose dependent inhibition of the castor oil induced diarrhoea [28] at the doses of 200 and 500 mg/kg as well as inhibition of the gastrointestinal propulsion of charcoal meal. This data corroborates the traditional usage of vinca in the treatment and management of diarrhoea [24].

6 Conclusion

Catharanthus roseus is one of the 21000 significant therapeutic plants found.

It can be considered as a rich source of alkaloids and phenolics, which possess diverse biological properties including anticancer, antidiabetic, antioxidant, antimicrobial and antihypertensive activities. Every part of *Catharanthus* like root, stem, bark and flower are rich sources of several bioactive compounds. It produces around 130 alkaloids, for example, reserpine, vinceine, raubasine and ajmalicine. Several studies already published on the alkaloids and their pharmaceutical properties however still more works are required to increase the production of these alkaloids at large scale.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors state that there are no personal, financial, or organizational conflicts of interest that may affect the output of this research.

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