

Study of Vinca Plant of Anticancer

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Date of Submission: 15-05-2024

Date of Acceptance: 25-05-2024

ABSTRACT

The Vinca plant, *Catharanthus roseus*, is a significant plant with a variety of medical use. People refer to it as Madagascar periwinkle. It is a little, native to the island of Madagascar, perennial herbaceous evergreen plant. Since it has been demonstrated to contain a variety of phytochemicals with a range of biological activities, including antioxidant, antibacterial, antifungal, antidiabetic, and anticancer characteristics, it has drawn more and more interest.

It contains approximately 130 alkaloids, mostly vinblastine, reserpine, vincristine, raubasine, and ajmalicine. It is noteworthy because the first plant-derived anticancer medicines used in clinical practice were vinblastine and vincristine, which were extracted from this plant. This paper summarizes the most recent methods for preparing dried material, extracting bioactive components from this plant, and isolating them. It also gives a summary of the traditional uses and phytochemical profiles of *C. roseus*. To support its potential as medicinal agents, the plant's extracts and bioactive components were also examined for their alleged health advantages.

Keywords: *Catharanthus roseus*, vinblastine, vincristine

I. INTRODUCTION

Vinca rosea is a significant medicinal plant that is a member of the Apocynaceae family. It is a dicotyledonous angiosperm with two alkaloids that are related to terpenes. That is the combination of vinblastine and vincristine used in cancer treatment. *Vinca* grows up to 500 meters in India. In the tropical and subtropical regions of south and northeastern India, it is grown without restriction. Its bloom has a darker red core and appears white to dark pink. Its corolla has five petals that resemble lobes and measures between 2.0 and 5.0 cm in diameter. The basal tube is 0.2 to 3.0 cm long. These fruit follicles measure between 2 and 4 cm in length and 3 mm in width when found in pairs (Manpreet Kaur, 2002). *Vinca* is also

known by the synonyms sadabahar, ratanjot, sadfuli, and *catharanthus roseus*.

HISTORY

Originating from the Greek words *katharos* (pure) and *anthos* (flower), Linnaeus developed the genus *Catharanthus*. *Catharanthus roseus* is the botanical name of *vinca*, as decided by the Scottish botanist George Don. This denomination has been the topic of many inquiries and heated discussions. In 1759, Swedish naturalist Carl von Linnæus was given the name *Vinca rosea*, the first species in his genus. The genus name *Lochnera* was proposed in 1828 by Heinrich Gottlieb Ludwig Reichenbach, a German botanist. In 1838, Austrian botanist Stephan Ladislaus Endlicher called the species *Lochnera rosea*.

William Stearn verified that the proper name for the Madagascan periwinkle is *Catharanthus roseus* in the botanical sense. Furthermore, the genus name *Lochnera* is invalid since it is too similar to the name of another genus, *Lochneria*, which was introduced in 1777 by the scientist Giovanni Antonio Scopoli, as noted by Stearn in his chapter "Synopsis of the Genus *Catharanthus*."

BOTANICAL CLASSIFICATION

Botanical Name(s): *Vinca Rosea* (*Catharanthus Roseus*)

Family Name: Apocynaceae

Kingdom: Plantae

Division: Magnoliopsida (Flowering plants)

Class: Magnoliopsida (Dicotyledons)

Order: Gentianales

family: Apocynaceae

Genus: *Catharanthus*

Species: *C. roseus*

VERNACULAR NAMES

English: Cayenne, jasmine, old maid

Hindi: Sada-bahar

Malayalam: Banappuva, Nityakalyani

Marathi: Sadaphool, Sadaphul

Sanskrit: Nityakalyani, Rasna,

Tamil: Cutkattumalli, Cutukattumalli

Telugu: Billaganneru

Gujarati: Barmasi

Bengali: Noyontara



Figure: Catharanthus Roseus



Figure: Vinca plant

BOTANICAL DESCRIPTION

- It is an herbaceous plant or an evergreen subshrub growing to 32 in 80 cm high. It has glistening, dark green, and flowers all summer long. The flowers of the naturally appear pale pink with purple “eye” in their centers. Erect or accumbent ufrutex, to 1 m, usually with white latex. Stems is green, often permeate with purple or red.
- Leaves: Oval leaves (1-2in long) decussate, petiolate; lamina variable, elliptic, obovate or narrowly obviate; apex mucronate.
- Flowers: 4-5 cm, classy, white or pink, with a purple, red, pale yellow or white centre Follicle 1.2-3.8 × 0.2-0.3 cm, susceptible on the axial side. Seeds 1-2 mm, are numerous and grooved on one side. Climate, soil and propagation
- Flowering period: Throughout the year in equatorial conditions, and from spring to late autumn, in warm
- temperate climates.
- Soil: Full sun and well-drained soil is preferred.
- Light: Bright light, included three or four hours of direct sunlight daily, is essential for good flowering.
- Temperature: Normal room temperatures is suitable at all times. It cannot tolerate temperatures less than 10°C (50°F).

MORPHOLOGICAL CHARACTERS

A vinca comes in white, blue, and purple hues. It's a kind of corneal or annular plant. Vinca leaves are oblong, ovate, glossy, bitter, and have a faint odor. The plant is roughly 0.52 to 1 cm long (erdogrul, 2002).

ORGANOLEPTIC CHARACTERS

The flowers are violet, pink, white, or carmine red in color, while the leaves are green and the roots are grey. The flavor is unpleasant and the smell is distinctive. Vinca has a pubescent, upright habit with a branching top root. Simple, petiolate, ovate, or oblong, unicostate, reticulate, whole, brittle, with a sharp tip and glossy look are the characteristics of leaves. Flowers are hermaphrodite, bractate, pedicillate, and complete; they often occur in lymose axillary clusters of two to three. Follicles with many black seeds are called fruits.

MICRO SCOPIC CHARACTERS

A single layer of rectangular-celled epidermis with unicellular covering trichomes is present on the upper surface. Under the upper epidermis, palisade is composed of a single layer with compact, longitudinally arranged cells. The five to eight layers of sponge parenchyma have gaps between the cells. Collenchymas are visible in the midrib both above and below the top and lower epidermis. There are phloem and xylem in the center.

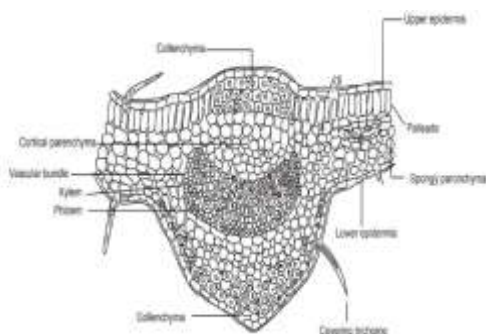


Figure: Microscopy of Vinca

CULTIVATION AND COLLECTION

Vinca grows up to 500 meters in India. It thrives in tropical and subtropical regions of south and northwest India, with the exception of extremely alkaline or wet soil. It thrives in light sandy soil that is high in humus. The ideal amount of rain is roughly 100 centimeters. Fresh seeds are used for propagation, and they are dispersed in nurseries. Direct seeding is also occasionally carried out. Approximately 2.5 kg of seeds are needed for each hectare during direct sowing. They are placed in rows 45 cm apart during the monsoon and combined with ten times the amount of sand.

After the plants reach a good size, they are thinned out, leaving around 30 centimeters between each plant. Nursery seeding is proven to be cost-effective. They are sown in nurseries in February or March and then moved to open fields. when they have been achieved, after two months.up to 7 cm in height.

They are moved to 45 cm by 30 cm open fields. It needs to be far away and have roughly 74,000 plants per acre. The plants are drought-resistant and don't require a lot of water. Through the plant doesn't need a specific fertilizer supply. Potassium, phosphorus, and nitrogen together produce good outcomes. Sometimes, farm yard manures are also employed.

when a year of growth, reading is conducted on a regular basis, and when the leaves, stems, and seeds are pulled out by ploughing, they are further cleaned, dried in shade, and packaged in bails. The leaf stripping is cut about 7 to 8 cm above the ground level.For the next propagation, the seeds from ripe fruits are collected. In irrigated land, the yield of dry roots, stems, and leaves per hectare is one to five land three tones, respectively.

CHEMICAL CONSTITUENTS

There have been reports of about 150 alkaloids from vinca. Alkaloids found in additional

genera of the family have been identified, including ajmalicine, lochnerine, vindoline, catharanthine, reserpine, serpentine, and tetrahydro alstonine. There are reports of about 20 dimetric alkaloids from the plants that have anti-neoplastic activity, such as leurocraistine (also known as vincristine in the US), vincalucoblastine (also known as vinblastine in the US), and vindescine.Vindoline and catharthine, two indole alkaloids that are found in plants, combine to form vinblastine.

Vincristine shares structural similarities with vinblastine; however, in the vindoline-derived form, the indole nitrogen has a formyl group rather than a methyl group. Chemically, vinblastine can be changed into vincristine. Since the alkaloid is found in very modest amounts—typically 0.85% in roots, 0.67% in leaves, and 0.31% in stems—nearly 500 kg of vinca are used to create 1 gram of vincristine by the utilization of the bacterium streptomycin albobrigriseolus driven n-demethylation process.

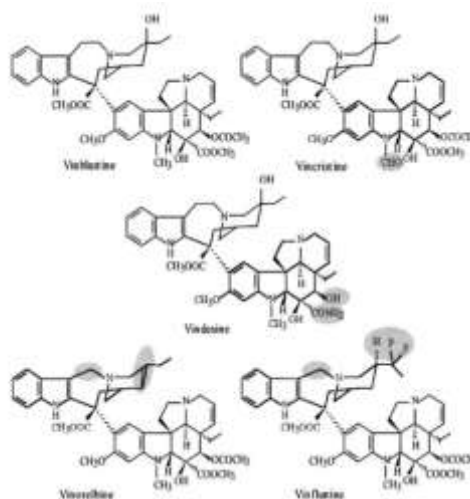


Figure: Chemical constituents

MECHANISM OF ACTION

Vinca cause cytotoxicity is due to their interactions with disruption of microtubule function and tubulin, especially of microtubules comprising the mitotic spindle fiber and causing metaphase arrest. They can perform some other biochemical response which can be effective or may not be effective on microtubules. Have some effect which donot interrupted the microtubule only after treatment of cells with clinically irrelevant doses of the vinca. Vinca and other anti-micro tubule drug are also showing effect on both malignant cells and non-malignant cells, in the non-mitotic cell cycle, because microtubules are involved in various non-mitotic functions.

Vinca are connected to binding sites of tubulin which is separate from the taxanes, colchicines, podophyllotoxin and guanosin-5'-triphosphate. binding occur rapidly and can reverse too. Maintains the existence of vinca binding site /mole of tubulin dimer. [16-17] high affinity binding sites in each microtubule which is located at the end of per microtubule. the vinca bind at the binding site and interrupts microtubule congregation, but low drug concentration can be decreasing the rates of both growth and shortening at the assembly end of the microtubule that can cause produces a "kinetic cap and suppress function". The disturbing effects of the vinca on microtubules dynamics, particularly at the ends of mitotic spindle, which causes meta phase arrest, occur at drug concentration below those that decrease microtubule mass. The vinca and other microtubule distort agents have power to inhibit malignant angiogenesis in vitro.

tumors. Vinblastine is utilized tentatively for treatment of neoplasms and is suggested for Hodgkin's sickness, choriocarcinoma.

C. roseus was found to show the noteworthy anticancer movement against various cell types in vitro condition and particularly most prominent action was found against the multidrug safe tumor types. Vinca alkaloids likewise called as mitotic axle harms, they restrain get together of the axle structures from microtubules, there by hindering mitosis in cell cycle. Vinca alkaloids subsequently effectively keep disease cells from partitioning. Distinctive Vinca alkaloids have their own special properties [17]. Vinca alkaloids square cells in mitosis since they are cell cycle explicit specialists. The vinca alkaloids tie explicitly to tubulin and obstruct its capacity to polymerize with a-tubulin into microtubules. Without a flawless mitotic axle, copied chromosomes can't adjust along the division plate and cell division is captured in metaphase. Cells obstructed in mitosis go through changes normal for apoptosis. They are additionally utilized for therapy of leukemias, lymphomas, and testicular disease.

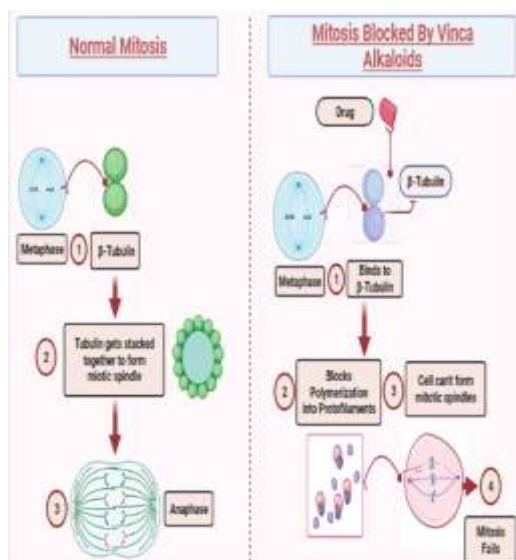


Figure: Mechanism of action Vinca alkaloids

PHARMACOLOGICAL ACTIVITY

1. Anticancer Activity

In clinical practice, the organization of C. roseus is done intravenously, after which they are in the long run used by the liver and discharged. Going bald, fringe neuropathy, obstruction and hyponatremia are the significant symptoms of this medications. To improve the remedial list, semi engineered Catharanthus alkaloids, for example, vinorelbine and vinflunine were created. Vinorelbine and vinflunine apply their antitumor impact by authoritative to tubulin. These alkaloids have development restraint influence some human

2. Antidiabetic Activity

Vinca rosea of flowers and leaves have ethanolic extracts which is similar to the standard drug glibenclamide which is a hypoglycemic agent. The Hypo glyceemic action has been arosed due to the result of the increase glucose utilization in the liver [7,8,9]. Due to utilization of glucose in liver ,hypoglycemic activity is been observed. Dichloromethane: methanol extract [1:1] has hypoglycemic activity on leaves and twigs of vinca in streptozotocin which induce diabetic rat model at the dose of 500mg/kg which is been admistered orally for 7-15days. . 48.6 and 57.6% hypoglycemic activity was observed and further treatment for a period of 30 days has provided complete protection against STZ challenge (75 mg/kg/i.p.). Glycogen synthase, glucose 6-phosphatedehydrogenase, succinate dehydrogenase and malate dehydrogenase are the enzyme activities which decrease the liver of diabetic animals and it is been improved after the treatment with extract at a dose of 500mg/kg oral for 7 days. it indicates the increase in the metabolized glucose in the rats which are been treated with increased lipid per oxidation levels.

3. Antimicrobial Activity

C. roseus has been found to be a significant restorative plant for the making of the

novel pharmaceuticals as the greater part of the bacterial microorganisms were improving obstruction against a considerable lot of the accessible enemy of microbial medications. Plants have been supported to be important regular assets for the dynamic chemotherapeutic operators and recommend a wide range of activity with the more prominent accentuation on the preventive activity [21]. It is exhibited that freak leaf extricates had great antibacterial potential against *S. aureus*, *S. citreus*, and *E. coli* and *P. aeruginosa* microscopic organisms while *B. subtilis* was not influenced. The vacillation in antibacterial movement among freak and control plant leaves may be expected to the genomic changes, stirred by the mutagen correspondingly affecting the combination and level of bio-dynamic mixes like vincristine, Vinblastine, vindoline in tissue, which may be commitment for antibacterial property of periwinkle leaves as additionally detailed before.

4. Anti-Diarrheal Activity

The in vivo anti diarrheal activity of *C. roseus* ethanolic leaf separate was tried in the Wistar rodents with castor oil as a test the runs initiating specialist notwithstanding the pretreatment of the concentrate. Loperamide and atropine sulfate were utilized as the standard medications. The counter diarrheal impact of ethanolic concentrate of *C. roseus* indicated the portion subordinate restraint of the castor oil actuated the runs at the dosages of 200 and 500 mg/kg. The concentrates essentially decreased the number and weight of wet fecal pellets with remove treated gatherings indicating lower diarrheal seriousness than control rodents incited the runs in Wistar rodents. A further dosage of 200 and 500 mg/kg of the concentrate hindered castor oil incited loose bowels just as repressed gastrointestinal drive of charcoal dinner. This information confirms the conventional utilization of *C. roseus* in the treatment and the executives of the runs.

5. Memory enhancement property

Vinpocetine has been reported to have a variety of actions that would hypothetically be beneficial in Alzheimer's disease (AD). The only study investigating this agent in a well-defined cohort of AD patients found no benefit. Metaanalysis of older studies of vinpocetine in poorly-defined dementia populations concluded that there is insufficient evidence to support its clinical use at this time. Vinpocetine has been well tolerated at

doses up to 60 mg/d in clinical trials of dementia and stroke, and no significant adverse events.

6. Anti-Helminthic Activity

Human beings and cattle are more prone for this chronic illness of helmenth infections. *Vinca* has anti-helmenthic property which is been evaluated by experipement model of pherithemapostuma and piperazine citrate as standard reference. 250mg/ml is the ethanolic extract for anti-helimenthic activity.

7. Wound Healing Property

Ethanolic extracts of 100mg/kg/day is given for rats which have wound gealing property. There is a decrease in epithelization period which has high rate of wound contraction, which is marked as an increase in dry weight and hydroxyproline. There is an increase in the tensile strength along with hydroxyproline which helps in management of wound healing together.

8. 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 animal.

9. Hypolipidimic 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.

10. 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

11. 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.

12. Anti-Oxidant Property

The anti-oxidant potential of the ethanolic extract of the roots of the varieties of vinca namely rosea (pink flower) and alba(white flower).

REVIEW OF ANTICANCER

Activity of Vinca According to Wilson et al One of the most effective anticancer drug targets is the highly active mitotic-spindle microtubule. Paclitaxel and Vinca alkaloids were once thought to function primarily by raising or lowering the cellular microtubule mass, making them microtubule targeted medicines. An increasing number of structurally unique peptides and depsipeptides identified from a variety of organisms have tubulin as their target. Since microtubules' subunit protein is tubulin, most compounds are highly toxic to mammalian cells.

Although these agents can be distinguished by their effects on microtubules and tubulin binding sites, the ultimate consequence is the same because microtubule disruption causes cell cycle arrest at the G2/M phase and apoptotic cell death as a result. The leaves and stems are the source of alkaloids that have anti-tumor and mostly anti-cancer property. Alkaloids inhibit the tumors. Vinblastine is used for the treatment of neoplasm of Hodgkin's disease, choriocarcinoma.

Vincristine is used for the leukemia in youngsters. Vinblastine is offered as Velban or Vincristin pills. To enhance the healing index, semisynthetic Catharanthus alkaloids along with vinorelbine and vinflunine were developed. Vincristine is used for the leukemia in children. Vinorelbine and vinflunine exert their antitumor impact by binding to tubulin.

The alkaloids are also called mitotic spindle poisons they inhibit the metaphase of microtubules which inhibit the mitosis in cell cycle. Hence vinca alkaloids help in preventing the cancer from further division. Researchers found that Vinca alkaloids have been found to cause the formation of tubulin spiral filaments. Also, there were four vinca alkaloids which inhibit the cellular uptake and tubulin binding characteristics. Later it was discovered that the anti-angiogenic effects in murine tumor models for anticancer activity.

According to research, intraperitoneal administration of vinblastine or colchicine to B6D2F1 mice with advanced subcutaneous colon tumors significantly slowed the growth of the tumors, and within 8 hours of therapy, hemorrhagic necrosis gradually developed. Vinflunine had superior in vivo experimental

antitumor activity when compared to vinorelbine in a panel of human tumour xenografts. Vinflunine, a novel Vinca alkaloid created from vinorelbine utilizing superacidic chemistry. As having a different mechanism of action from vinorelbine in preclinical tumour models. Vinblastine has varied effects on polymerization and dynamics at opposing microtubule ends.

Vinca alkaloids cause tubulin to form ordered paracrystals and indeterminate spirals that compete with the development of microtubules. The discovery that the Vinorelbine (VLB) group of alkaloids are known as "spindle poisons" due to their ability to obstruct tubulin's ability to polymerize, which is a protein necessary for the formation of the microtubule system, which is crucial for nerve conduction, as well as the mitotic spindle, which manifests during cell division. 20 Synthetic derivatives were prepared wherein Anhydrovinblastine N-oxide 4 was subjected to the modified Polonovski reaction and found that the resulting reaction medium produced 5'-nor anhydrovinblastine after hydrolysis., the resulting compounds showed anticancer activity.

Further it was discovered that Vinca rosea Linn's anticancer principles have an experimental basis for clinical examination. The structure-activity correlations of dimeric Catharanthus alkaloids have been the subject of diligent effort. Vinorelbine, synthesized by C' ring contraction of anhydrovinblastine, is currently sold all over the world thanks to Fahy J et al. tireless efforts to discover novel chemistry that allowed the semi-synthesis of derivatives changed in the velbenamine "upper" end of the molecule.

The pharmacology, physicochemical factors, naturally occurring bisindole alkaloids from Catharanthus, modifications of the upper half (velbanamine portion) of bisindole alkaloids, modifications of the lower half (vindoline portion) of bisindole alkaloids, multiple modifications: 4'-epideoxyvincristine, and new concepts in medicinal chemistry of bisindole alkaloids are all discovered by him. Further the successful molecular constructions included additional three-membered rings into the 14,15-position of the vindoline component of the dimer alkaloid by the Simmons-Smith reaction.

This led to the synthesis of cyclopropanated vinblastine and its derivatives. In the presence of diethylzinc, reactions with iodoform and bromoform, respectively, were used to produce halogenated 14,15-cyclopropanovindoline. 25,26 Alkaloid Vinorelbine

(VLB) caused C-mitosis in vivo in both the normal rat bone marrow and the cells of the L1210 ascites tumour.

Post-metaphase completely vanished as a result of the afflicted cells being halted in metaphase. Stages of the prophase were unaffected. Tryptophan or glutamic acid treatment can change how VLB affects the production of metaphase arrest. It was further discovered the Vinorelbine effect on cells expanding in tissue culture. J-96 and LLC-He1 cells treated with VLB experience metaphase arrest and characteristic C-mitotic chromosomal alterations.

Acute lymphoblastic leukaemia (ALL), malignant lymphoma, and neuroblastoma are only a few of the cancers that are frequently treated using done work on Vincristine (VCR), an alkaloid derived from vinca. Further it was noted reported and discovered that the anti-cancer medications taxol, vincristine, and cisplatin clinically induce severe sensory neuropathy in addition to autonomic neuropathy. Although experimental sensory neuropathies brought on by these anti-cancer medications have been discovered to be prevented by nerve growth factor (NGF) administration, and to state that information about autonomic neuropathy is sparse.

II. CONCLUSION

Vinca has been shown to possess life-saving qualities in the majority of cancer patients. It possesses both anticancer and anti-tumor capabilities. Vinca's semi-synthetic derivatives have a well-established track record of anticancer efficacy, and the crude extract is no exception. Furthermore, it falls within the category of cytotoxic drugs like vinblastine, vincristine, and vinorelbine that have FDA approval. More drugs, like vinflunine, are being developed to treat urothelial transitional carcinoma as a second-line treatment. According to the overall assessment of research, vinca has the potential to be an effective ethnopharmacological anticancer drug.

ACKNOWLEDGMENT

With great pleasure and profound sense of gratitude, Miss. Shamili Singh Assistant Professor of LCIT School of Pharmacy for his/her valuable guidance, keep interest, inspiration, unflinching encouragement and moral support throughout my major project report work.

I especially indebted to my mentor Dr. (Mrs.) Shruti Rathore, Professor/ Principal, LCIT School of Pharmacy, Bilaspur (C.G.) who offered

her continuous advice and encouragement throughout course of this thesis.

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