

A review article on Ophthalmic Preparation by Using Transitional Metal Complex Synthesised from Hedychium Coronarium Leaf for the treatment of Diabetic Cataract

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ABSTRACT

Diabetes cataract is one the most common endocrinological disorder which is globally affecting a large number of the persons. Uncontrolled diabetes may trigger secondary delirious complications affecting the kidneys, eyes, cardiovascular system and central nervous system. Elevated blood glucose level causes detrimental secondary ocular complications like diabetic cataract, diabetic retinopathy, diabetic keratanopathy, diabetic glaucoma and diabetic papillopathy. In this work we evaluated the role of the nicotine exacerbation on the diabetic cataract and evaluated the pharmacological approach in management of the diabetic cataract using transitional metal coordination complex.

The extensive literature survey was done to find suitable candidates for the ligand and metal ion for the metal coordination synthesis which not only manage the diabetes but also improves the damage done to the lens due to cataract caused by diabetic cataract.

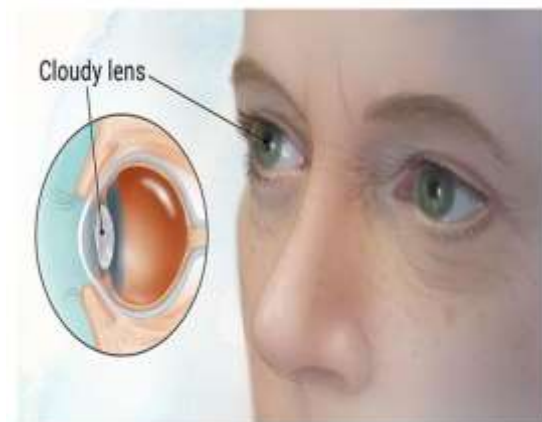
The rationale behind selecting the transitional as metal ion for the complex was the insulinomimetic effect of transitional metal salts and NSAID was selected because of the previous reported beneficial effects of NSAID against diabetic complications due to reduction in oxidative stress as well as in inflammatory mediators like interleukins. The complex was synthesized using as metal ion and NSAID as the ligand. The synthesized complex was evaluated for physiochemical properties and structural confirmation. The current work also explore the role of ophthalmic drug delivery system effect against diabetic cataract, to design a system with maximum effect and minimum obnoxious effects.

KEYWORDS: Diabetescataract, Insulinomimetic effect, NSAID, Ophthalmic drug delivery system.

INTRODUCTION

In various studies it has been reported that cataractogenesis secondary to the diabetes is one of the most common ocular complications. The oxidative stress that arise due to hyperglycemia leads to development of cataract. The condition of diabetic cataract gets worst when nicotine is consumed concurrently. Cataractous-opacification of the lens results in 50% of global blindness. In current scenario surgical extraction of the opaque lens followed by intraocular lens implantation (implanting with a polymer lens) is the only remedy available another drawback associated with surgical approach for management of cataract is the post-surgical complications like macular edema, posterior capsular opacification, retinopathy, photopsia and ptosis. There is no evidence till date that affirms the fact that conventional anti diabetic drugs completely cure the diabetes as well as improves secondary complications like cataractogenesis.

Ultimately conditions finally need cataract surgery, which produces complications. The current need of the hour is the development of empirical pharmacological therapy that has maximum benefits and minimum obnoxious effects, so that the shortcoming of the current surgical therapy could be overcome against diabetic cataract exacerbated by nicotine. The current work has been done with the perception of synthesizing transitional metal complex with NSAID and comparing its efficacy against diabetic cataract which is exacerbated diabetic cataract.



CATARACT

Cataract is a word derived from the Latin, 'cataracta' meaning 'waterfall' and the Greek 'katarrhaktes', from katarassein means "to dash down". Cataract is defined as opacification of the lens and loss of transparency of the lens in the eye as a result of tissue breakdown or protein clumping. World Health Organization (WHO) had defined cataract as a visual acuity (VA) of less than 3/60 in the better eye and which is considered as one of the leading cause of blindness in the world. One of the current studies predicts that cataract is responsible for 51% of world blindness. Cataract is considered as a major public health problem worldwide, particularly in developing countries of Asian subcontinent. The prevalence of blindness in developing countries is 10 to 40 times higher than in developed countries.

Cataract development is usually a very slow or gradual process but in some cases the process of cataractogenesis occur rapidly and generally both eyes are affected. The total number of subjects with cataracts is estimated to rise to 40 million by 2025.

Cataract formation or lenticular opacity is a normal age dependent process, occurring mainly in the geriatric population. There are many factors like diabetes, smoking, alcohol and nicotine abuse, hypertension, UV radiations which worsens the cataractogenic formation. There are no absolute remedies available for solving the problem of cataractogenesis. Surgical approach is generally considered for management of diabetic cataract. In previous studies by various researchers it was found that before, during and after the cataract removal by surgical approach the chances of secondary complications like optic nerve damage, globe perforation, zonular dialysis, iris prolapse, postoperative uveitis, infectious endophthalmitis, toxic anterior segment syndrome (TASS), and

posterior capsule opacification (PCO) were significantly high. The human ocular lens is transparent, biconvex, elliptical organ located in the visual axis of the eye between anterior aqueous humour and posterior vitreous humour. The anterior surface of the lens is lined by a single layer of the lens epithelial cells (LEC). In the equatorial region of lens, these LEC terminally differentiate to form lens fibers which do not possess any nucleus and cell organelle. The absence of nucleus and cell organelles, on one side, mean crystal clear transparency of the lens but, on other side the lens fibers lose machinery that keeps them metabolically active. The opacification of the lens fibers in any region of lens is called cataract which is a leading cause of visual impairment throughout the world. Based on the region of opacification cataracts are mainly of threetypes.

CATARACTS ARE MAINLY OF THREE TYPES

1. Nuclear Cataracts.
2. Cortical Cataracts.
3. Posterior Sub-capsular Cataracts (PSC).

NUCLEAR CATARACT

Nuclear cataracts are the most common type of cataract and are usually associated with aging. A nuclear cataract occurs in the center of the lens.

CORTICAL CATARACT

Cortical cataracts are often found in people with diabetes spokes in the cortex (softer material surrounding the innermost nucleus of the lens) of the lens.

This type of cataract progresses, with spokes extending from the outside of the lens to the center.

POSTERIOR SUBCAPSULAR CATARACT

Sub-capsular cataracts are found in people with diabetes, as well as those with high myopia (near-sightedness), retinitis pigmentosa, or steroid intake.

This type of cataract develops slowly and starts as a small opacity under the capsule, usually at the back of the lens.

Common

More than 1 million cases per year in India

- ✓ Treatable by a medical professional.
- ✓ Requires a medical diagnosis.
- ✓ Lab tests or imaging not required.
- ✓ Chronic: can last for years or be lifelong.

- ✓ Most cataracts develop slowly over the course of years.
- ✓ The main symptom is blurry vision.
- ✓ Having cataracts can be like looking through a cloudy window.

PREVALENCE AND INCIDENCE

Several previous reports give details about the prevalence and incidence of cataract worldwide.

- “Prevalence” is the total number of people having cataract in a population at a given time.
- While, “Incidence” means the number of new cases that occur over a given period of time.

They have correlated the incidence of cataract with age.

There was a steep rise in cataract incidence after the age of fifty that leads to 4 million blindness per year **Incidence of blindness by cataract in India**

Age group (in years)	Incidents (per 10,000 population p.a)
35-39	190
40-44	253
45-49	595
50-54	1336
55-59	2388
60-64	3734
65	5860

DIABETIC CATARACT

Diabetic cataract is formed due to increase in sugars in the lens. The excess amount of sugar within the lens is reduced by aldose reductase enzyme to its corresponding alcohol. The capsule of the lens is relatively impermeable to sugar alcohols, the lens imbibes water, causing osmotic imbalance.

Pathogenesis of Diabetic Cataract

Aldose reductase is an enzyme in the polyol pathway that causes formation of sorbitol by reduction of glucose molecule, which is an important step in the development of diabetic cataract. A cataract due to sugar formation takes place due to intracellular accumulation of sorbitol leading to osmotic change resulting in a hydropic lens having a high degenerative effect.

Sorbitol is rapidly produced and converted to fructose by the enzyme sorbitol dehydrogenase in the lens. A hyperosmotic effect is created due to increased sorbitol accumulation resulting in a fluid infusion to counteract the osmotic gradient. In previous pre-clinical experimental studies it was observed that intracellular polyol accumulation leads to liquefaction and collapse of fibers present in the lens, leading to formation of lens opacities. These postulates had led the foundation of “Osmotic Hypothesis” of diabetic cataract formation, elaborating the role of intracellular elevation in the fluid level as a result of aldose reductase mediated polyol accumulation, causing swelling in the lens accompanied by complex biochemical changes, resulting in cataractogenesis.

In further studies it has been observed that accumulation of the sorbitol caused osmotic stress in lens, causing apoptosis in the epithelial cells of the lens (LEC), resulting in cataract formation. In a study it was found that hyperglycemic transgenic mice which over express phospholipase D (PLD) and aldose reductase (AR) genes were more prone to the diabetic cataract in comparison to the diabetic mice that over express phospholipase D (PLD) genes only. Phospholipase D (PLD) is the key enzymes that play a vital role in the lens osmoregulation. The above mentioned results confirms that osmoregulation impairment in the lens, develops a condition in the lens that slightest elevation in the aldose reductase cause significant increase in the osmotic stress, leading to progressive cataractogenesis. Osmotic stress plays a vital role in rapid cataractogenesis in young type-1 diabetes mellitus subjects causing cortical lens swelling. These results asserts that osmoregulation impairment may render the lens susceptible to even minimum increases of aldose reductase directed osmotic stress, ultimately leading to progressive cataract formation.

Osmotic stress plays a pivotal role in rapid cataractogenesis in young type-1 diabetes mellitus subjects resulting in cortical lens fibers swelling.

In a study by Oishi et al it was investigated about the contribution of aldose reductase in formation of adult diabetic cataracts. Level of aldose reductase in red blood cells of subjects below age group of 60 years and having short duration of diabetes were found to be directly related with formation of posterior sub capsular cataracts (PSC). In diabetic subjects an inverse relation between the amount of aldose reductase enzyme in the erythrocytes and the lens was observed, it was also noticed generally that the diabetic’s subjects have less epithelial cell density

in the lens as compared to the non-diabetic subjects indicating the substantial role of aldose reductase enzyme in pathophysiological mechanism of cataractogenesis.

Polyol pathway is considered to be the cardinal pathway for the oxidative stress in the lens, arising secondary to the diabetes. Osmotic stress in the endoplasmic reticulum(ER) [major cell organelles for protein synthesis] was initiated due to accumulation of sorbitol, ultimately leading to generation of free radicals.

Glucose level fluctuations cause stress in the endoplasmic reticulum, starting an unfolded protein response which results in generation of reactive oxygen species ultimately damaging the lens fibre, due to oxidative stress.

In various recent publications it was observed that oxidative stress caused lens fibre damage due to free radical scavengers in diabetic subjects, yet no conclusive evidence that indicates that the free radicals initiates the cataractogenesis process but their role in acceleration and worsening of the cataractogenesis could be preceidental. In various previous studies it was observed that in aqueous humor of the diabetic subjects, there is substantial increase in the hydrogen peroxide (H₂O₂) level, leading to formation of hydroxyl radicals formation (OH⁻) following the entry through lens, the whole process mentioned above is generally known as “Fenton reaction”. The elevated level of nitric oxide free radical (NO•) in diabetic lens and in aqueous humor results in increment in peroxy nitrite formation, causing cellular damage due to its oxidizing properties.

Metal Coordination compounds as pharmaceutical agents

The use of metal as pharmaceutical agent had been an important field. It had fascinated the researchers from ancient times. There are three major parts in any metal coordination complex they are:-

- [1] Metal ions: - The positively charged group that accepts the electron.
- [2] Ligands: - The negatively charged ions that donates the ion.
- [3] Coordinate or Dative bonds: - which shares the electrons

Generally the d-block of the periodic table has the capability to form the coordinate bonds as they have variable valances and thus also known as transition metals.

Metal compounds as anti-diabetic agents

Many metal complexes have been synthesized and evaluated to overcome the short

comes of painful insulin injection and side effects for type 1/type 2 diabetes mellitus (DM). Although, many metal ions like chromium, manganese, molybdenum copper [Wang et al 2014], cobalt, zinc and vanadium ions have been reported in many studies to exhibit insulin-mimetic or enhancing properties in vitro and in vivo. Vanadium seems to be the most promising and the most explored one, especially when coordinated to certain organic ligands. The insulinomimetic effects of vanadium salts on cells and diabetic animals have stimulated years of research into the clinical use of vanadium compounds as insulinomimetic.

Vanadium as lead compound for diabetes and its ocular complications

Andrés Manuel Del Río in 1801 first discovered Vanadium. He originally named the element as “pan chromium” due to spectrum of colors associated with various oxides of the metal, but changed the name to “erythronium,” as most of the mineral salts turned red upon heating. Del Rio was later convinced by fellow scientists that he had really found impure chromium and not a new element. Later the same element was “rediscovered” 30 years by Swedish chemist, Nils Gabriel Sefstrom, who named it vanadium, after the Nordic goddess of beauty, Vanadis.

Vanadium nutritionally is thought to be an important cofactor in various enzymatic reactions. Various previous data from animal and human studies suggest vanadium mimics the action of insulin. It was found that it may serve a beneficial role in promoting healthy glucose metabolism in individuals with diabetes or dysglycemia. Dietary sources that are rich in vanadium include mushrooms, shellfish, black pepper, parsley, dill seed, and grains.

Vanadium in some animals is considered as one of the most important essential nutrient. One of the example that asserts about the importance of vanadium in animals is the role of vanadium in the diets of chickens whose deficiency had an adverse effect on bones, feathers, and blood. In human subjects, classification of vanadium as an “essential nutrient” is still a matter of research debate among various research groups.

Some group of researchers consider vanadium to be an ultra-trace element in human, requiring dietary intake of 20 mcg per day only. Certain mushrooms species for example Amanita muscaria whose one of the main constituents is amavadine, (S,S)-2,20-(hydroxyimino) dipropionic acid, is a natural, vanadium-containing compound

which is thought to be a oxidation mediator of thiol compounds with carboxylic or ester groups, like cysteine and glutathione.

Various different forms of vanadium are used in foods or in form of supplements, or they may be found in drinking water. An average human diet supplies 6-18 mcg of vanadium per day, with an estimated only five percent of ingested vanadium which being absorbed. In vivo vanadium is converted to a vanadyl cation where it can form complexes with biological substances such as ferritin and transferrin. In the body the highest concentrations of vanadium are found in the liver, kidney, and bone.

In an animal study of radio-labelled vanadium administered using i.v. injection, it was observed that the element, at least in this form, was poorly absorbed by the tissues, and was mainly urine excreted. Vanadium appears to be affected by the plasma insulin.

Aspirin and its anti-cataract effects

Various previous epidemiological studies indicated that regular use of aspirin-like analgesics decreases the incidence of cataract and further epidemiological work supported the theory that those subjects who consume aspirin regularly are less likely to need cataract surgery. Aspirin is a potential candidate for anti-cataract agent since it has relatively few side effects and inexpensive. Aspirin is prescribed as a remedy or prophylactic for a large range of disorders. Cotlier and Sharma in 1981 was the first to suggest that aspirin might be the cause of decrease in lens opacification in rheumatoid arthritis subjects. An elevated level of plasma tryptophan and its metabolites have been found in the subjects of senile cataracts and the of the amino acid cataractogenic effect had been the probable reason. Smith and Lakatos found a decrease of 47% in bound plasma tryptophan after oral administration of 1800 mg of aspirin, indicating that aspirin may affect the human lens by lowering plasma tryptophan level. It was further mechanisms by which aspirin exert its effect:

- (a) Via modification in glucose metabolism,
- b) Changes in the physical behaviour of proteins within lens fibers or
- (c) In the communication between lens epithelial cells.

Disorder in each of these processes is associated with lens opacification and can be modified by aspirin.

Investigators also suggested that the mechanism behind the inhibitory effect of aspirin

might be through acetylation of the lens proteins, perhaps by competing with carbamylation glycosylation or steroid binding. It has been reported that aspirin can acetylate a variety of proteins which include lens proteins. Aspirin has been shown to prevent protein carbamylation; hence causing cyanate- induced phase separation temperature and lens opacification. The tight binding of labeled aspirin to lens protein and the preincubation results indicated that aspirin exerts its protective effect by itself reacting with the protein amino group to prevent attack by cyanate. Presumably the reaction is the transfer of acetyl group from aspirin to protein's amino groups. The inhibitory effect of acetylation by aspirin appears to be mediated through a blockage of amino groups that are involved in glycation. In non-enzymic glycosylation of bovine lens proteins, the protection against the reaction was shown by aspirin (acetyl salicylic acid), but not salicylic acid, which is structurally identical except for the absence of acetyl group showing that acetylation may play a role in the protection.

PLANT PROFILE



Figure: Hedychium coronarium
Family-Zingiberaceae

Plants are used as rich source of medicine since ancient time. Scientific exploration of traditional knowledge of use of herbs in treatment of various ailments is one of the thrust areas of

research. Herbal medicines are in great demand and in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs. *Hedychium coronarium* plant is widely utilized in traditional medicine systems where it grows, although applications vary by region. This plant has tremendous medicinal properties and its various parts are used in traditional as well as modern medicine². The rhizome of the plant is used in the treatment of diabetes, cold, body aches, headache, lancinating pain, contusion, inflammation and rheumatic pain. The rhizome has anti-cancerous, antioxidant, anti-hypertensive, diuretic, leishmanicidal, anti-malarial activities and also used in irregular menstruation, piles bleeding and stone in urinary tract. Recently, antifungal activity of *Hedychium coronarium* crude extracts was reported. The extracts are as good as or even better than standard drugs like statin and griseofulvin. Cancer chemoprevention activity is also reported recently of labdanoid terpenes from rhizomes of *Hedychium*⁶. The medicinal value of this plant in the treatment of a large number of human ailments is mentioned in Ayurveda, Charaka Samhita and Sushruta Samhita. *Hedychium coronarium* plant (Family-Zingiberaceae) also known as the White Ginger Lily or Dolanchampa or kapur kachri is a vigorous all-growing ginger from the Himalayas and consists multiple stems per pot. It is hard, perennial, erect, branched, annual weed up to 3-6 feet height. The leaves are simple arranged in alternate manner with undulate margin. The flowers are white in color and have pleasant fragrance; summer flowering; fall flowering. The trunk is green in color, very thick. It is widely distributed over the tropical and subtropical region of the Asia and Africa. It is an annual branching herb which grows well on wastelands and in tropical region after the rainy season⁸. Though the plant is traditionally used in many parts of Bangladesh, no scientific report is available to validate the folkloric use. Again, plants have been a promising source of drug molecules for ages. Bangladesh is blessed with rich floristic resources. Still the untapped wealth of plant kingdom is a major target for the search of new lead compounds in drug discovery.

Synonyms

Hindi: Dolanchampa, Gulbakawali, Kapoorkachari, Manipuri: Takhelleiangouba, **Marathi:** Sontakka, Kannada: Surulisugandhi, Malayalam: Kalyanasauganthikum, **English:** White ginger, butterfly ginger, butterfly lily, cinnamon,

jasmine, garland flower, garlandlily, ginger lily, white butterfly ginger, white butterfly ginger lily, white garland lily.

Cuba: Mariposa blanca literally white moth flower, Spanish: Guajiro's, Brazilian name: Liriodobrejo.

Taxonomical Classification

- Kingdom: Plantae
- Subkingdom : Angiosperm
- Class: Monocots
- Order: Zingiberales
- Family: Zingiberaceae
- Subfamily: Zingiberoideae
- Genus: *Hedychium*
- Species: *coronarium*
- Binomial name : *Hedychium coronarium*

Botanical Description

This herb is perennial, erect, unbranched, up to 3-6 m high, growing from a rhizome. Leaves are simple, alternate, two-ranked, sessile at the top of the leaf sheath, blade elliptic to lanceolate, 20-30 x 3-10 cm, pubescent on lower surface. Flowers are continuously through the year; flowers many, in groups of one to six, borne among large, green, overlapping bracts in an ellipsoidal spike 7-20 cm long at the apex of the inflorescence, fragrant. Corolla with fused tepals, white, the tube narrow, 6-9 cm long, the segments linear, 3-5 cm long with two petal-like oblong lobes. Stamens 3.5-5.5 cm long and a petal-like, sub round, apically notched labellum slightly longer with a yellowish green or dull white patch in the center. Fruits are oblong, many seeded, capsule. It is widely distributed over the tropical and subtropical region of the Asia and Africa. It is an annual branching herb which grows well on wastelands and in tropical region after the rainy season. It favors wet habitat, rain forest, moist forest, roadsides, open areas, streamsides.

Pharmacological Activities

Its rhizome is used in the treatment of diabetes. Traditionally it is used for the treatment of tonsillitis, infected nostrils, tumor and fever. It is also used as anti-rheumatic, antioxidant, excitant, febrifuge, and tonic. It has been reported that the essential oil extracted from leaves, flowers and rhizome of the plant have molluscicidal activity, potent inhibitory action, antimicrobial activities, antifungal, anti-inflammatory, antibacterial and analgesic effects. The seeds are aromatic, carminative and stomachic. The plant also possessed analgesic and neuro-pharmacological, anti-inflammatory, antimicrobial and cytotoxic

activities. This plant has tremendous medicinal properties and its various parts are used in traditional as well as modern medicine. The rhizome of the plant is used in the treatment of diabetes, cold, body aches, headache, lancinating pain, contusion, inflammation and rheumatic pain. The rhizome has anti-cancerous, anti-hypertensive, diuretic, leishmanicidal, anti-malarial activities and also in irregular menstruation, piles bleeding and stone in urinary tract.

Hedychium coronarium is a perennial medicinal herb which is distributed in throughout the world and used as traditional medicine since the ancient time. It contains various bioactive compounds including Phenols, Terpenoids, Saponins, Volatile oils, Flavonoids, Glycosides etc. These bioactive compounds made this herb as a valuable potent herbal drug. Hedychium coronarium has high ethno medicinal significance in India and China as well. H. coronarium is endemic in the Amarkantak area of Central India. Due to over-exploitation of this plant for extraction of crude drug (Eye Tonic), it is rapidly disappearing from its natural habitat at alarming rate and needs urgent protection and conservation. In present article medicinal, pharmacological and other important properties of Hedychium coronarium were compiled. Review reveals this plant as potent herbal drug and remedy for many ailments.

Butterfly ginger lily is beautiful and fragrant flower native to East India. It is a robust, attractive plant that will reach 6 feet in containers. Leaves are lance-shaped and sharp-pointed, 8-24 in long and 2-5 in wide and arranged in 2 neat ranks that run the length of the stem. From midsummer through autumn the stalks are topped with 6-12 in long clusters of wonderfully fragrant white flowers that look like butterflies. The flowers eventually give way to showy seed pods chock full of bright red seeds. The rhizomes of Butterfly ginger lily (called loklei) are used in Manipur in the preparation of traditional dish called as eromba. Butterfly ginger lily is found in the Eastern Himalayas, from Nepal, to Sikkim and NE India, and also Western Ghats, at altitudes of 800-1900 m. It is also found in SE Asia, and is widely cultivated as a garden plant.

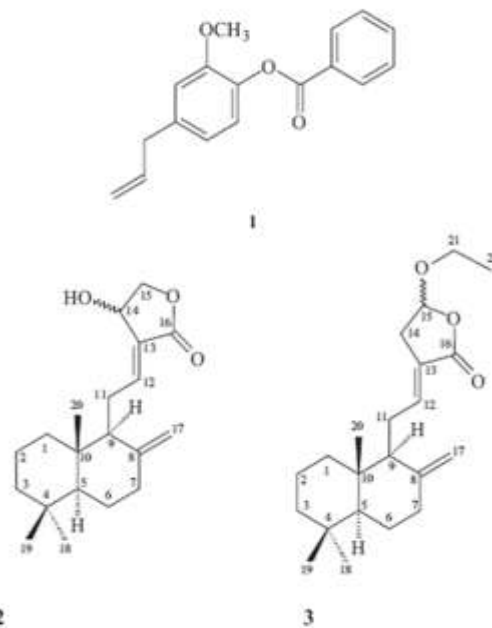
Phytochemical Characteristics

Hedychium coronarium contain many bioactive compounds including a ponins, glycosides, fats and volatile oil. The main chemical found in the plant include hedychicoronarin, peroxyconararin D, 7 β hydroxyl-calcaratararin A and E, 7 β -hydroxy-6-oxo-labda-8, 12-diene-15, 16-dial

have been isolated from the rhizomes of Hedychium coronarium.

Hedychicoronarin, peroxyconararin D were isolated as optically active colorless oil. The phytochemical study of the rhizomes from Hedychium coronarium showed the presence of benzoyl eugenol along with the labdanediterpenesis coronarin D and ethoxy coronarin D also. Hedychium coronarium afforded oils whose major constituents were β -pinene (20.0 %), linalool (15.8 %), α -pinene (10.1 %), 1,8-cineole (10.7 %) and α -terpineol (8.6 %) in the leaf while the root consists mainly of β -pinene (23.6 %), α -humulene (17.1 %), β -caryophyllene (13.0 %), α -pinene (6.9 %) and elemol (6.9 %). The volatile constituents of the various parts of H. coronarium from other parts of the world have been reported. Although ubiquitous on terpenes and sesquiterpenes were the main components of these oils, the identities of these compounds differed from one another. This led to the delineation of various chemotypic forms of the essential oils of H. coronarium. The compositional pattern of the leaf oil (β -pinene, linalool, α -pinene, 1,8-cineole) and the root (β -pinene, β -caryophyllene, α -humulene) in this study seems to be new chemotypic forms of essential oil of the plant when compared with previous studies.

In the Figure



1. Hedychicoronarin
2. Peroxyconararin D,
3. 7 β hydroxyl-calcaratararin

HEDYCHUM CORONARIUM

Common name	Butterfly ginger, butter lily, ginger lilies
Botanical name	Hedychium coronarium
Family	Zingiberaceae
Sunlight	Full sun, partial sun
Height	24 to 150 inches
Water	Medium
Maintenance	Medium

Hedychium coronarium is a robust and attractive plant that can grow upto 6 feet tall in a container. The lance-shaped, sharp-pointed leaves of this plant range in size from 8 to 24 inches in length and 2 to 5 inches in width, and they are placed in two tidy ranks along the length of the stem. Midway through summer and into autumn, the stalks are crowned with long clusters of 6-12 inches in length of incredibly fragrant white blooms that resemble butterflies. In time, the blossoms will be replaced by a display of seed pods bursting with vibrant crimson seeds.

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