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PHYTOCHEMISTRY AND PHARMACOLOGICAL POTENTIAL OF ALOSCASIA MACRORRHIZA: A COMPREHENSIVE REVIEW

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ABSTRACT
Background: *Aloscasia macrorrhiza*, commonly known as Giant Taro, is a species rich in phytochemicals with diverse pharmacological properties. Phytochemical analysis shows different bioactive compounds like alkaloids, flavonoids, terpenoids, phenolics, and saponins in different components of the plant body, including leaves, stems, and roots. Alocasin, a class of alkaloids, is most prominent in this plant. These substances are likely responsible for different biological activities, as *Aloscasia macrorrhiza* shows. **Aim**: This review unveils the phytochemical composition and pharmacological activities of various parts of *Aloscasia macrorrhiza*. **Method**: Multiple Literature, including research and review papers, were searched for based on their title, abstracts, and keywords. Keywords like '*Aloscasia macrorrhiza*,' 'Phytochemistry,' 'Traditional uses,' and 'Ethnomedicinal uses' were used to collect information. Abstracts of articles with relevant titles were screened, and the full text was considered. Only articles published from 2018 to 2024 were considered. Based on their classes and mechanistic actions, this review consolidated these phytoconstituents. **Results**: These phytoconstituents exhibit a wide array of therapeutic activities, including anti-inflammatory (due to tannins and polyphenols), antimicrobial (due to terpenes and lectins), antioxidant (due to polyphenols), anticancer (due to flavonoids), anti-diabetic (due to flavonoids) effects. **Conclusion**: This review provides insights to the therapeutic potential of *Aloscasia macrorrhiza* and hence forms a bridge of understanding between the traditional uses and the modern Pharmacology studies. In the future, further clarification and detailed mechanistic insight can be done. *Aloscasia macrorrhiza* may have potential therapeutic applications and is subject to further investigation.

INTRODUCTION

Since ancient times, plants have been the most trusted source of treatment for all sorts of diseases. Even now, most people believe more in herbal products than chemically synthesized compounds to alleviate diseases [1]. In an era where the search for novel, effective, and safe therapeutic agents is of utmost

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importance, the plant remains the hub of multiple unexplored bioactive compounds that can be used to treat diseases. Detailed insight into traditional medicine systems provides a valuable starting point for modern pharmacological investigations, potentially leading to developing new drugs or nutraceuticals [2]. Even now, according to WHO, 80% of common people depend on natural products to treat their diseases.

Recent advances in High throughput screening with sophisticated chromatographic and spectroscopic techniques, such as HPLC-MS and NMR, enable screening of potential bioactive compounds [2,3]. It is estimated that only a small fraction of the world's plant species have been systematically investigated for bioactive compounds. The vast reservoir of compounds and phytoconstituents are yet to be explored for beneficial uses [4].

The Araceae family comprises over 3700 species. Among all, giant taro or *Aloscasia macrorrhiza* shows a wider and more diverse composition of phytoconstituents and pharmacological activities [5]. Other Araceae species, like *Colocasia esculenta* and *Amorphophallus spp.*, have high nutritional content, mainly due to their mineral, oxalate, and flavonoid content. However, *A. macrorrhiza* has more biological activities due to multiple classes of phytoconstituents, mainly mono galactosyl diacylglycerol, distinguishing it from other species. Unlike *Zantedeschia aethiopica*, it shows potent antioxidant potential due to many polyphenolic compounds and flavonoids. Like *Typhonium flagelliforme*, it has a cytotoxic effect and potent anticancer agent due to Lectins, which induces apoptosis. Giant taro is an even more potent anti-inflammatory and anti-microbial agent due to the presence of tannins and terpenes, respectively. Unlike other plants of the same family, *Aloscasia macrorrhiza* is a potent antidiabetic agent too [5].

Since *Aloscasia macrorrhiza* combines multiple biological uses and traditional uses of multiple species of the Araceae family, this review aims to discuss the phytochemistry and pharmacological action of *Aloscasia macrorrhiza* with its mechanistic insight. The unclear mechanistic insights of different phytoconstituents from different scientific papers have been compiled. While different papers have highlighted specific phytoconstituents and their mechanistic approach, a gap exists in correlating traditional uses to modern Pharmacology. This review forms a bridge between traditional folklore and modern scientific knowledge.

Taxonomic Classification

Aloscasia macrorrhiza belongs to Streptophyta (Phylum), Magnoliopsida (Class), Alismatales (order), Araceae (Family) and genus Aloscasia (Genus) [6].

Habitat and Distribution

Natively, *Aloscasia macrorrhiza* is found in South Eastern Asia and the Pacific region. It is abundantly found in tropical climate regions, including India, Bangladesh, and Myanmar, where soil has a higher content of water [7]. It is extensively found in the sub-tropical region of Japan and China [8]. Aloscasia shows vegetative reproduction with the help of a rhizome. Due to this ability, these plants can spread rapidly to form their colony. New plants originate from the tubers, which grow along to develop their new habitat. The enriched phytoconstituents, nutrient composition, and traditional uses make Aloscasia a commonly found plant in India, Bangladesh, Myanmar, and Sri Lanka.

Morphology of *Aloscasia macrorrhiza*

Aloscasia is found all around the year and thus is a perennial plant. Because of their enormous shape and size, they are named giant taro. Giant taro can be up to 4 or 5 meters tall when fully grown. Thus, they are the largest species in the *Aloscasia* genus [9]. They have long petioles and long-leave stalks. As discussed earlier, their roots are in the form of rhizomes. This rhizome is responsible for their rapid vegetative propagation [9,10]. Leaves are broad and can grow as long as 1.5 meters in length. Sagittate in shape, they have an upper glossy structure due to a thicker cuticle layer, preventing water loss by transpiration. The lower surface, however, is hairy and uneven [10]. The family Areaceae and the genus *Aloscasia* is unique for their inflorescence. It comprises a spadix, which is a flower-like, and collar-like spathe, which are petals. Thus, spathe encloses the spadix. These plants have both male and female parts in the same flower [11].

Synonym

Aloscasia macrorrhiza is commonly known by various names. In English, it is called Giant taro or elephant ear; in Bengali, it is called Mankachu, and in Sanskrit, it is called Mahakanda or Vrihatkanda.

Traditional Use and Importance

The importance of *Aloscasia macrorrhiza* as an essential source of bioactive compounds originated because of its diverse use in traditional medicine. Research is ongoing to fill the gaps

between traditional knowledge and the reasons associated with biological activity. Table 1 mentions different important traditional uses of Aloscasia macrorrhiza. Because of their traditional importance, the quest to derive the mechanism of action for these biological effects has led to several research studies. This review paper aims to encompass several research papers to gain deep insight into different phytoconstituents and pharmacological effects shown by *Aloscasia macrorrhiza*.

Table 1: Ethnomedicinal uses of *Aloscasia macrorrhiza*

S No.	Disease	Parts used	Reference
1.	Laxative, Pain reducing in Rheumatoid Arthritis, analgesia; Diuretics	Leaves	[12]
2.	Gastrointestinal ailments, including diarrhea, dysentery, and stomach ulcers	Rhizome	[13]
3.	Reduce constipation	Leaves and stems	[13]
4.	Rubefacient	Leaves and roots	[14,15]
5.	Treat constipation; edema	Root and stem (tuber)	[13,12]
6.	Gout and rheumatism	Tuber	[16]
7.	Rheumatic pain	Tuber	[16]
8.	Constipations and piles	Tuber	[13]
9.	Menstrual disorders and postpartum complications	Tuber	[8,15]
10.	Mouth ulcer	Root	[12]
11.	Toothache	Petioles	[12,17]
12.	Cough and otorrhea	Petioles	[12]
13.	Treat cuts, wounds, and skin infections in Polynesian medicine	Sap from petiole	[8,14,15]
14.	Headache	Sap of petiole	[16]
15.	Laxative	Stem	[13]
16.	Treat scorpion stings	Stem	[18]
17.	Cough and respiratory problems	Stem, rhizomes	[18]
18.	Inflammation, eczema, and abscess	Rhizome	[14]

PHYTOCHEMISTRY OF *Aloscasia macrorrhiza*

Recent advances in chromatographic methods like HPTLC and HPLC allow the separation of different components present in extracts for further analysis. The extracts are mainly made up of different solvents like ethanol, methanol, and chloroform by maceration, digestion, or solution. The separated components are then analyzed using different techniques like NMR, MS, or hyphenated techniques, where separation and identification are done at the same time [2].

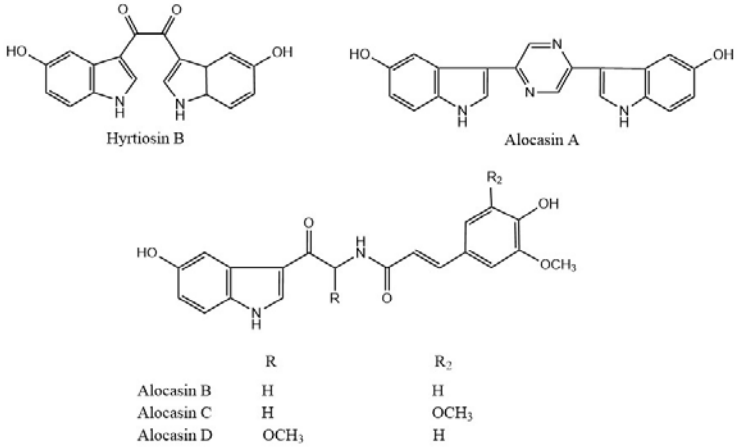

Figure 1: Important alkaloids found in *Aloscasia macrorrhiza*

The major phytocomponents involve alkaloids. These alkaloids were extracted using chloroform as a solvent using a maceration technique at room temperature. The extracted components were separated by HPTLC and identified by NMR. Generally, reverse

reverse-phase HPTLC C-18 columns were used to separate the alkaloids with ethyl acetate, methanol, and ammonium hydroxide in a ratio of 40:10:10 v/v were used [15]. The main alkaloids are Alocasin, which is represented in Figure 1. Four different alocasin are found in *Aloscasia macrorrhiza*, which are Alocasin A-D [19]. The structures of other important phytoconstituents are represented in Figure 2.

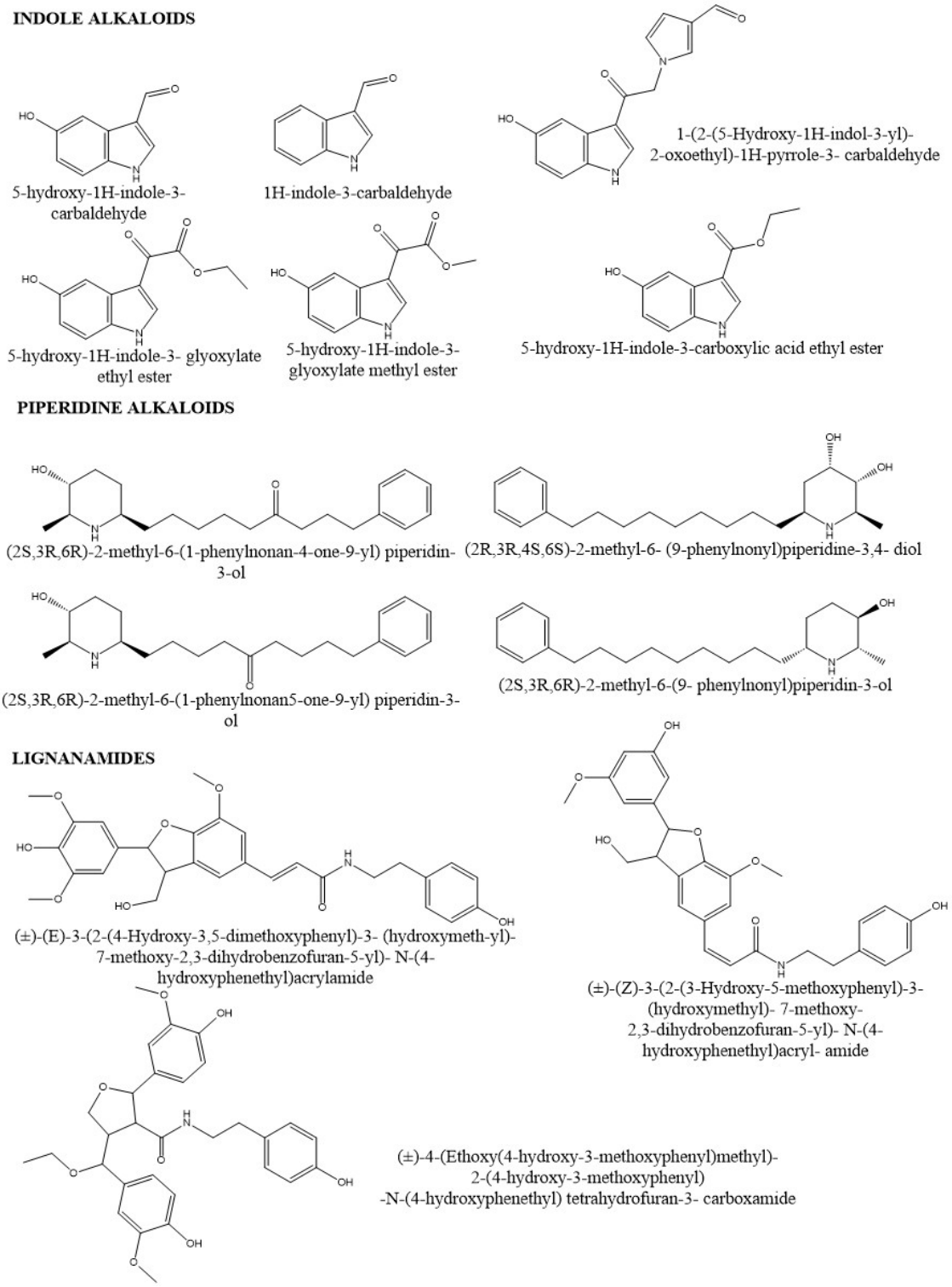

Figure 2. Important phytoconstituents present in *Aloscasia macrorrhiza*

The different phytochemical constituents deduced by different analytical techniques and structural elucidation are mentioned in Table 2 below.

Table 2: Different classes of phytoconstituents found in *Aloscasia macrorrhiza*

S No.	Class of compounds	Name of the compounds	Occurrence
1	Alkaloids	**Main alkaloids** [19]**:** Alocasin A – E Hytiosin B β-adenosine 2-(5-Hydroxy-1H-indol-3yl)-2- oxo-acetic acid Hyrtiosulawesine	Ethanolic extract of the rhizomes
		Indole alkaloids [19]**:** 1-(2-(5-Hydroxy-1H-indol-3-yl)-2-oxoethyl)-1H-pyrrole-3-carbaldehyde Grossamide (cis and trans) 5-hydroxy-1H-indole3-glyoxylate methyl ester 1H–indole-3-carbaldehyde 5-hydroxy-1H-indole-3- carbaldehyde 1H–indole- 3-carboxylic acid 5-hydroxy-1H-indole-3-carboxylic acid ethyl ester	
		Piperidine alkaloids [20]**:** (2S,3R,6R)-2-methyl-6-(1-phenylnonan-4-one-9-yl) piperidin-3-ol (2S,3R,6R)-2-methyl-6-(9- phenylnonyl)piperidin-3-ol, (2S,3S,6S)-2-methyl-6-(9- phenylnonyl)piperidin-3-ol, (2R,3R,4R,6R)-2- methyl-6-(9-phenylnonyl)piperidine-3,4- diol	
2	Lignanamides [21]	(±)-(Z)-3-(2-(4-Hydroxy-3,5-dimethoxyphenyl)-3- (hydroxymeth-yl)-7-methoxy-2,3-dihydrobenzofuran-5-yl)- N-(4-hydroxyphenethyl)acrylamide (±)-(Z)-3-(2-(3-Hydroxy-5-methoxyphenyl)-3- (hydroxymethyl)- 7-methoxy-2,3-dihydrobenzofuran-5-yl)- N-(4-hydroxyphenethyl)acryl- amide	Ethanolic extract of the rhizomes
5	Anthocyanins [22]	Cyanidin 3-rutinoside	Petiole
6	Flavonoids [23]	Quercetin Quercetin 3O-glycoside Apigenin 5C-glycoside Kaempferol Cyanidin	Methanolic extract of the leaves
7	Sterols [21]	3-Epi-ursolic acid 3-Epi-Betulinic acid β-Sitosterol β-sitosterol 3-O-β-D-glucoside	Methanol extract of the rhizomes
8	Cyanogenic glycosides [24]	Triglochinin isotriglochinin	Leaves
9	Sphingolipids [23]	1-O-β-D- glucopyranosyl-(2S,3R,4E,8Z)-2- [(2(R)–hydroctadecanoyl)amido]-4,8-octadecadiene-1,3- diol	Methanolic extract of the rhizomes
10	Ceramide [25]	(2S,3S,4R)-2N-[(2′R)-2′- Hydroxy-hexacosanoyl]- tetradecane-l,3,4-triol (alomacrorrhiza A)	Ethanolic extract of the roots

Pharmacological activities of *Aloscasia macrorrhiza*

Biological activities elicited by a specific plant part are called pharmacological activity. The activity shown is by a particular phytoconstituent or in conjugation with other phytoconstituent. These phytoconstituents interact with our body in several ways to elicit or inhibit different pathways and thus show several biological activities. The main Pharmacological activities shown by other parts of *Aloscasia macrorrhiza* are mentioned below:

Antioxidant activity

Oxidation is a chemical reaction that involves the loss of electrons from a chemical species. Several reactions occur in our body where different chemical species are oxidized to form free radicals. These are called auto-oxidation [26]. This causes the progression of cellular and tissue damage. Free radical scavengers are antioxidants that destroy free radicals so that their injurious effect on tissue and cells is limited. This free radical scavenging is required to balance ROS and antioxidants properly. Some important enzymes used in free radical scavenging include Superoxide dismutase, glutathione peroxidase, and catalase [27]. *Aloscasia* species contain multiple components which are polyphenolic in nature. These polyphenolic compounds donate protons to the free radical species to convert them to stable organic compounds.

This free radical scavenging method is categorized under the antioxidant activity of different components. Phenolic compounds like Flavonoids can scavenge ROS or Reactive Oxygen Species, which are mainly radicals of Hydroxyl along with Superoxide and Hydrogen peroxide, and stabilize different lipid free radicals caused by lipid peroxidation. [28]. Polyphenols stabilize free radicals by donating a hydrogen atom or electron. Hydroalcoholic extract composed of 70% methanol and 30% water of leaves of *Aloscasia* species was made, and the extract was tested for antioxidant activities at a dosage of 200-1000μg/ml [28]. The activity of the extract against different chemical samples was observed, taking ascorbic acid as the test sample. Ascorbic acid, or Vitamin C, is a prominent antioxidant with multiple uses in free radical scavenging. Vitamin C acts as a proton donor to stabilize the highly reactive species of free radicals. The stabilized species does not cause cellular or tissue damage. This Vitamin C is again converted back to the protonated form in vivo [29]. This Vitamin C scavenges the free radical, converting it to a stabilized form, thus quenching oxidative stress. The different test samples used are:

1. 2,2-diphenyl-1-picrylhydrazyl, commonly termed DPPH, is a common test to check the antioxidant potency of different plant extracts. This compound contains Nitrogen, which is a free radical. Thus, this free radical inside the body can cause oxidative stress and cellular damage. In the presence of an antioxidant, the DPPH is converted to DPPHH or 2,2-diphenyl-1-picrylhydrazine, a protonated and stable complex form. This is an *in-vitro* test for antioxidant potency. The DPPHH shows its absorbance maxima at a wavelength of 517nm. The extract of *Aloscasia* showed a rapid increase in the percentage scavenging of free radicals up to 600μg/ml forming a plateau phase. The antioxidant activity of 200μg/ml extract is found to be similar to 200μg/ml standard ascorbic acid solution [28].
2. In the presence of free radicals, when cellular damage occurs, the glucose uptake to the cell by the GLUT-4 receptor comparatively reduces due to tissue damage. Thus, the concentration of glucose in the bloodstream increases. This causes an increase in the concentration of glucose attached to hemoglobin. This raises the level of HbA1c and forms glycosylated hemoglobin. This is even an early sign of diabetes [30]. The percentage of scavenging increased slowly by a dose-dependent increase of the extract of the leaves of the *Aloscasia* species. Activity of 1000μg/ml was found to be similar to 200μg/ml ascorbic acid [28].
3. Hydrogen peroxide forms hydroxyl radical by Fenton reaction. The ferrous ion is converted to a ferric ion in the Fenton reaction. Thus, there is an increase in oxidation stress or a loss of electrons. This helps gain electrons by the hydrogen peroxide forming hydroxyl radical. This hydrogen radical causes direct cellular injury and tissue damage [27]. Studies reveal that the radical scavenging property of 200μg/ml ascorbic acid was similar to 100μg/ml of hydroalcoholic extract of the leaves with insignificant differences in ANOVA studies with a P value of 0.143. Gradually, it showed a slight rise in the antioxidant activity curve of the leaf extract [28]. This signifies that this plant is a potent antioxidant.

Moreover, it was found that the alcoholic extract possesses higher antioxidant potential than hydroalcoholic or aqueous extracts. The scavenging of DPPH to DPPHH of ethanolic extract was almost 3.5 times the aqueous extract. Assay result shows that alcoholic extract also contains a higher content of enzymes that contain antioxidant activity like Superoxide dismutase and catalase enzyme [31].

Anti-diarrheic activities

Pathology is defined as an abnormal physiology. Diarrhea is a common pathological condition that is seen mainly in developing countries. Poor hygiene and rapid contamination are the main causes of this disease. Diarrhea is characterized by watery stool, which is caused by either reduced water absorption from stool or due to increased water secretion, causing diarrhea [32]. The basic mechanism of diarrhea can be described in the following steps:

a) Ingestion of toxins, pathogens, or microbial species is mainly responsible for secretory diarrhea. Consumption of various food substances that contain microbial species is a major cause of gastrointestinal infections, followed by diarrhea. *Salmonella* species from eggs and milk, *Campylobacter* species from milk, poultry, meat, and other microbes cause Diarrhoea [33].

b) This toxin or organism causes colonization in the large intestine and the bowel tract. This colonization causes inflammation followed by toxin elaboration. The increased inflammation causes the secretion of inflammatory mediators, which reduces water reabsorption from the bowel

c) The toxin binds to the receptors of the enterocyte. Enterocytes are the microvilli extensions present more abundantly in the small intestines than the large intestine, increasing the intestine's surface area for better water and electrolyte reabsorption from the bowel.

d) This increases the concentration of the different intracellular mediators, which include cAMP and cGMP. This activates the targets like Phosphokinase A, activating the Phospholipase C. The PLC activation causes an increased calcium signaling pathway where Ca^{2+} influx increases [34].

e) This alters the porin channel, transporter protein, and the symport anti-port complex. Hence, it prevents the reabsorption of water or electrolytes from the bowel and secretes water from the intestinal lumen to the bowel tract, which causes diarrhea.

Two important models that illustrate diarrheic activities are magnesium sulphate and castor oil. Castor oil is shown to cause diarrhea due to one of its essential constituents, ricinoleic acid. Thereby increasing the bowel fluidity and bowel movement. Thus, causing diarrhea [35]. Magnesium sulphate induces diarrhea by reducing or inhibiting water and electrolyte reabsorption from the bowel, causing a loss of electrolytes and water from the body.

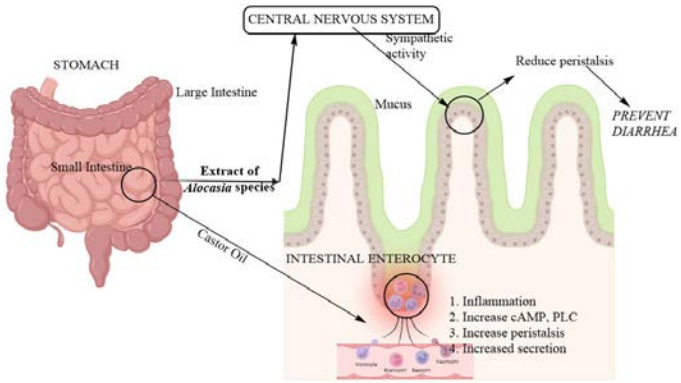

Figure 3: Anti-diarrheic action by *Aloscasia macrorrhiza*

The anti-diarrheic activities of *Aloscasia macrorrhiza* were tested using the leaf extract. Both ethanolic and aqueous extracts of the leaves were made. *Aloscasia macrorrhiza* showed anti-diarrhea activities in vitro and in vivo by multiple mechanisms, as shown in Figure 3.

a) In pathological diarrhea conditions caused by toxins or pathological microbes, it has been seen that the alcoholic extract of *Aloscasia* tuber shows dose-dependent inhibition of the growth of the pathogen. This inhibition of microbial growth inhibits further microbial colonization in the intestinal mucosa and thereby shows anti-diarrheic activity [15].

b) Castor oil mice model in-vivo shows that increased Prostaglandin increases the peristaltic movement of the small intestine. Alcoholic extract of *Aloscasia* species counteracts the activity of ricinoleic acid and activates sympathetic activity. The sympathomimetic activity reduces peristalsis and thereby reduces the diarrheic effect of Castor oil. The fluid accumulation in the lumen of the small intestine is also inhibited by the alcoholic extract, which is caused by ricinoleic acid. Hence, it shows anti-diarrhea action [32]. Species containing ricinoleic acid show anti-diarrhea action. However, synergistic action with alocasin makes *A. macrorrhiza* a more potent anti-diarrheic agent.

c) When compared to 400mg/kg dose of loperamide, with alcoholic extract of the tuber of the plant, the anti-diarrheic action can be found [15,32].

The anti-diarrheic action is due to different components like alkaloids, flavonoids, and saponins.

Anti-microbial activity

Antimicrobial activity is the ability to retard or prevent microbial growth in the human body. Antibiotics are derived from living organisms that, at a given concentration, inhibit growth or kill

the growth of microorganisms in the human body to prevent further infections [36,37]. Studies reveal that different extracts of leaves of the *Aloscasia* species in various solvent systems are found to be different. For example, when leaf extract of concentration 500mg/ disk leaf of chloroform, ethanol, and ethyl acetate was applied to the culture of *Bacillus megaterium*, the zone of inhibition was found to be 10, 12, and 8mm, respectively. This illustrates that the rate of penetration and diffusion of the components of different extracting mediums in the same bacterial cell is different [38].

Similarly, *Shigella dysentery*, a Gram-negative bacterium, shows a different zone of inhibition when the disk was subjected to leaf extract of *Aloscasia* species in chloroform ethanol and ethyl acetate. The zone of inhibitions was found to be 14, 10, and 12mm [38]. The antibacterial activity is defined by minimum inhibitory concentration (MIC). The MIC is the minimum component concentration required to inhibit or prevent microbial growth. Extracts of leaf, root, and stolon of *Aloscasia* species on *Pseudomonous aeruginosa* showed MIC of 128, 64, 128 μg/ml, indicating the antibacterial potential of stolon and leaf is the highest [38]. An anti-bacterial assay was conducted, which suggests that leaf and tuber extract (400μg/disc) of different solvents of *Alacosia* species shows considerable anti-microbial activity [39]. Taking chloroform as the solvent, the zone of inhibition was mainly shown for Gram-negative bacteria. Thus, chloroform extract can't enter Gram-positive bacteria. Carbon tetrachloride and methanol extract of the leaves showed a considerable diameter of the inhibiting zone for Gram-positive bacteria like Staphylococcus aureus, with 14.1 and 9.1mm diameters, respectively. The standard drug taken was Ciprofloxacin (5μg/disc), which showed about 32.7mm zone of inhibition [39]The P value in ANOVA studies was 0.08215, which is greater than 0.05 and proves no significant difference in the antimicrobial activity of A. macrorrhiza and the standard antibiotic Ciprofloxacin.

Anti-fungal activity

It has been evident that alcoholic extracts of tubers, leaves, and roots of Aloscasia species contain anti-fungal activity. This activity might be due to several mechanisms, including inhibition of hyphae growth to prevent an increase in fungal growth or by preventing ergosterol biosynthesis, which indicates fungicidal activities. Several researchers have demonstrated this activity in their research work.

1. Anti-fungal assay was conducted by disc diffusion method, where different extracts of leaves of *Aloscasia* were taken [39]. Two major fungi strains taken for the test were *Candida albicans* and *Aspergillus niger*, which in the human body is seen to cause Candidiasis and Aspergillosis, respectively. The plant extract was taken at a concentration of 400μg/disc against the standard drug ciprofloxacin (5μg/ml). The zone of inhibition by the standard drug for the two microbial species was found to be 34.8 and 45.4mm, respectively. The plant's chloroform extract and carbon tetrachloride extract failed to show any zone of inhibition on the disc, indicating the extracted component does not contain any anti-fungal activity. On the other hand, the Petroleum ether and Methanol fractions of the extracts showed the zone of inhibition for *Candida albicans* and *Aspergillus niger* for 11.9, 9.5, and 10.7, 7.7mm, respectively.
2. Studies illustrate the anti-fungal activity of different leaf extracts of *Aloscasia* species on different fungal strains like *Saccharomyces cerevisiae* and *Aspergillus niger* [32]. The anti-fungal tests were carried out in the sabouraud medium. The different solvents used to prepare the leaf extracts were aqueous solution, acetone, ethanol, and chloroform at 5 and 10mg/ml concentrations. The standard drug substance used to compare the test result is fluconazole (0.5mg/ml), which showed a zone of inhibition of 24.2mm. The zone of inhibition formed for 5mg/ml extracts of chloroform, water, acetone and ethanol were 15.2, 11.2, 14.1, 16.3mm for *Saccharomyces cerevisiae* and 10.3, 10.2, 11.2 and 13.4mm for *Aspergillus niger* while the standard showed zone of inhibition of 24.3 and 20.1mm respectively. This test proves that leaf extract of the plant species has anti-fungal activity against different common fungus which causes infection. The comparative activity of each of the extracting solvents is significantly different in both cases, since the P value of ANOVA for Saccharomyces cerevisiae and Aspergillus niger is 0.000416 and 0.00416, respectively.

Anti-diabetic activity

Diabetes mellitus is a common endocrine disorder characterized by deficient or impaired insulin release from the pancreas. Ironically, it affects about 6% of the world's population [40]. The insulin released from the pancreas binds with the tyrosine kinase insulin receptor. As this receptor undergoes auto-phosphorylation, it signals to the liver to convert the excess glucose in the blood to glycogen reserves [41,42]. It also signals

adipose tissue and skeletal muscle tissue cells to reuptake more glucose through the specialized glucose transporter (GLUT4) [43]. Type I DM is an autoimmune disorder, and the only treatment is Insulin replacement Therapy. At the same time, Type II DM can be maintained using proper diet, lifestyle habits, anti-hyperglycemic drugs, or insulin intake [44]. The phytochemical screening of *Aloscasia macrorrhiza* has led to the identification of different Alkaloids, Flavonoids, and steroids, which may play a crucial role in alleviating hyperglycemia. Experiments have been done with the ethanol extract of *A. macrorrhiza*, which has been shown to produce anti-hyperglycemic activity.

The study was conducted on 25 albino mice equally divided among 5 groups. Group I was the normal control and was injected with only the vehicle Dimethyl Sulfoxide; group II was the diabetic control; thus, neither the extract nor the standard drug was injected. To group III, the standard drug of Metformin was injected intraperitoneally (150mg/kg), and to group IV and V, the extract was injected at two different concentrations of 250mg/kg and 500mg/kg, respectively. After 16 hours, the results were analyzed. The effect of the extract of 250mg/kg was not statistically significant (41.70%); however, the concentration of 500mg/kg was highly significant (55.49) when compared to the reference drug (66.13%). The anti-hyperglycemic activity of the extract is shown by its stimulation of the β-cells of the pancreatic islet of Langerhans, thus secreting more insulin in the body. Alkaloids like Alocasin A, B, and E and Flavonoids like Quercetin and Quercetin 3-O-glycoside do this. Further, the insulin binds with the receptors and undergoes downstream signaling via the PI3K/Akt pathway. The signal is then transduced and stimulated in the liver to convert excess glucose into glycogen by glycogenesis [45].

The alcoholic extracts of leaves of *A. macrorrhiza* also showed anti-hyperglycemic activity against streptozotocin-induced hyperglycemia. The experiment was performed with 7 groups of rats. Group I was the normal control and thus received a normal diet, while the remaining groups, groups II to VII, were administered streptozotocin. Group II was diabetic control and received neither the extract nor the reference drug. Group III and IV received the leaf extract of concentration of 200mg/kg and 400mg/kg respectively. Similarly, Group V and VI received the stem extract of concentration of 200mg/kg and 400mg/kg, respectively, and Group VII received the reference drug Glibenclamide. The drugs were administered once daily for 21 days. After 21 days, the results were analyzed. It was found that both the leaves and stem extract showed significant anti-hyperglycemic activity ($p<0.05$) when differentiated from the reference drug. The main mechanism was hypothesized to be the presence of Alkaloids like Alocasin B, C, and E and Hyrtiosulawesine, which increases glucose uptake by the liver, thus inhibiting gluconeogenesis and also the secreted insulin binds with the GLUT4 glucose transported to facilitate increased glucose intake by direct stimulation of adipose tissue and skeletal muscle tissues thereby reducing blood glucose in the body [46].

Experimental studies with concentrations of 100mg/kg and 200mg/kg ethanolic extracts of *A. macrorrhiza* rhizomes were also shown to suppress glucose levels in the blood along with decreased levels of triglycerides in Streptozotocin & Nicotinamide induced hyperglycemia. The mechanism was hypothesized to be the availability of anti-inflammatory flavonoids like Apigenin 5C-glycoside, Kaempferol, and Cyanidin to modulate the inflammatory pathways, and thus insulin resistance is improved [47]. The detailed mechanism of anti-hyperglycemic action is shown in Figure 4.

Anticancer activity

Cancer is characterized by the abnormality of cells resulting from mutations in the genes, thus leading to altered cellular functions [48]. Cancer affects a wide range of populations all over the world, with men particularly suffering from prostate, lung, colon, and rectum cancers; women mainly suffer from breast, uterine, and thyroid cancers, while blood and cancers of the brain and lymph nodes are particularly affecting the children. [49]. The gene responsible for suppressing tumors, p53, helps in promoting normal growth and cellular divisions [50], [51]. They halt the cell cycle at different phases like G1 and G2 and so that the proper replication of the DNA can be ensured before finally advancing to the further stages of the cell cycle. However, if DNA damage is found during the replication process, it attempts to repair the DNA. If the DNA is irreparable, the cell undergoes programmed cell death or Apoptosis. The p53 gene is assisted by Cyclin-dependent kinase 1 (CDK1) during the process of cell cycle regulation [52]. But if, unfortunately, the p53 gene is mutated, then the CDK1 is overexpressed, and the cells with damaged DNA are resistant to apoptosis and continue to proliferate continuously [53].

The anticancer activity of *Aloscasia macrorrhiza* is due to the presence of different Alkaloids belonging to the chemical classes of Indole and Piperidine, cyanogenic glycosides, sphingolipids, and lignanamides. Studies have shown that the ethanolic extract of the *A. macrorrhiza* rhizomes has alkaloids like Hyrtosin B, Hyrtiosulawesine, and Alocasin A to E, which differ in their chemical structures based on the presence of H or methoxy (-OCH3) as their side groups. The experiment was performed on human hepatocarcinoma cell lines, Hep-2 and Hep-G2, with Doxorubicin as the reference drug using the MTT method. The Methyl thiazolyl Diphenyl tetrazolium bromide (MIT) technique is based upon the ability of the live cells to change the color of the yellow reagent of MIT to purplish crystals. The amount of viable cells is based on the intensity of the purple color [23]. Hyrtiosulawesine showed lenient anti-cancerous action on Hep-2, while Alocasin A and D showed gentle antiproliferative action on Hep-G2. These were compared with the reference drug of doxorubicin, which showed IC50 of 8.4, 7.2, and 8.8 µM against Hep-2, Hep-G2, and CNE, respectively. IC50 is the concentration of the test compound to eliminate 50% of the cell lines. The total RNA was retro-transcribed to cDNA via RNeasy Minikint. Apoptosis-related genes like Clydin D1, PPARγ, Bax, Bcl-2, and caspase 3,6,7 were quantified by using RT-PCR. Glyceraldehyde 3-phosphate dehydrogenase was utilized as the control [23].

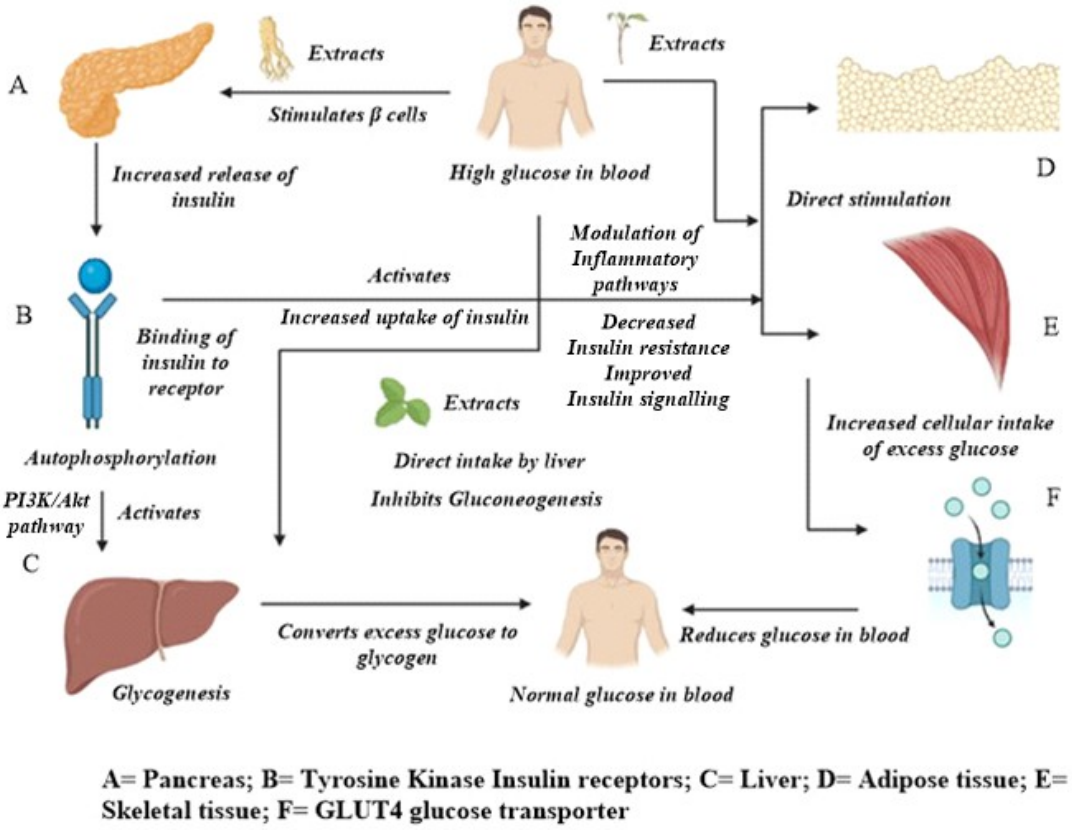

Figure 4. Mechanism of anti-diabetic effect of *A. macrorrhiza*

Studies have been conducted with ethanolic extract of *A. macrorrhiza* rhizomes on human hepatocarcinoma cell lines Hep-2 and Hep-G2, human colorectal carcinoma cultured cell lines HCT-116 and carcinoma cell lines MCF-7 using MTT method with 5-fluoro uracil as the reference drug. The results were analyzed to reveal that the IC50 of the extract was 7, 16, 8, and 18 µg/ml for Hep-2, HePG2, HCT-116, and MCF-7, respectively. The IC50 of 5-FU were 5, 8, 5, and 6 µg/ml in the same order. However, when individual components were tested on the cell lines, the IC50 of two components was lower than 5-FU. The caspase activity assays were done to quantify caspase 3,7 responsible for the activity. The components are α-mono palmitin, a bis-indole alkaloid, and 3-epi-betulinic acid, a sphingolipid that inhibits tubulin polymerization. It is likely to be the main mechanism of anticancer activity of the bis-indole alkaloids [20].

Another experiment has been done with the whole water extract of roots of *Aloscasia macrorrhiza*. BALB/c mice were chosen for this experiment, and 4T1 breast cancer cultured cell lines were used to induce the tumor in the mice. The five groups of mice were formed, starting with group I being the negative control receiving only saline water, group II was the positive control, and received Lentinan, which is an essential immune-modulating drug. Groups III to V received the AM extract of concentrations ranging from 16 mg/Kg body weight, 8mg/Kg body weight, and 4mg/Kg body weight, respectively. The size of the tumors was measured every 4th day, and after 21 days, the mice were sacrificed, and the weights of the tumor and spleen were measured. The results showed that the AM extract with the highest concentration significantly reduced tumor weight (96.7mg) which is 40% less than the negative control (160.7mg). it also showed a decrease in tumor size almost equal to the positive control (107.4mg). The medium and the low dose did not produce significant results. A flow cytometry assay was used to quantify apoptotic cells like Bax, Bak, Bcl-2, and caspase 7. The results also showed an increase in the size of the spleen, which is hypothesized to be the cause of the anti-cancerous activity of *A. macrorrhiza* [54]. Invitro studies have been done with the tuber of *Aloscasia macrorrhiza*, where ethanolic extract has been prepared. Standard human liver cell lines (L02) and Hepatocellular cellular carcinoma cell lines (SMMC-7721) were collected and seeded in wells. The *A. macrorrhiza* extract was then seeded with them at different concentrations, gradually increasing from 100 to 500 µg/ml. The results proved that the extract provided inhibitory action ($p<0.01$) of IC50 at 414µg/ml on cancerous cells and 1462 µg/ml for normal cells. The extract concentration of 500 µg/ml showed maximum inhibition of >80% of the cancerous cell lines [55]. Table 3 elaborates on the mechanistic insight into different Pharmacological activities and the components responsible.

Table 3: Mechanism of action of different Phytoconstituents of *Aloscasia macrorrhiza*

S No.	Pharmacological effect	Mechanism of effect	Phytoconstituent responsible	Parts of the plant found	Reference
1	Antioxidant effect	Free radical scavenging by H-donating; reducing oxidative stress; Stimulates antioxidant enzymes like SOD, catalase, and glutathione peroxidase	Flavonoids (quercetin, kaempferol), phenolic compounds	Leaves, Rhizome	[28,54,56]
2	Anti-diarrhea effect	Inhibition of intestinal motility by reducing Ca influx; Reduction of fluid accumulation in intestinal lumen; antagonize castor oil induced diarrhea mechanism	Tannins (gallocatechin, epigallocatechin); Alkaloids (alocasin, macrorrhizine)	Rhizome	[15,32,56]
3	Anti-bacterial effect	Components bind to bacterial ribosomes, preventing translation; Disrupting bacteria cell membrane; Disrupts cell wall formation by preventing peptidoglycan formation	Monoterpenes (limonene, α-pinene); Sesquiterpenes (β-caryophyllene); Flavonoids (chrysin); Lectin	Leaves, Stem	[38,39,57]
4	Anti-fungal effect	Ergosterol biosynthesis inhibition by triterpenes, Chitin synthase inhibition and antagonism	Alocasin; Triterpenes (oleanolic acid, ursolic acid); Saponins (alocaside)	Rhizome, leaves	[58]
5	Anti-diabetic effect	Improve glycolysis; Acts on Glut-4 receptor; Inhibits gluconeogenesis	Quercetin and other flavonoids	Tuber	[45,46]
6	Anti-neoplastic effect	Induce apoptosis by activating MMR gene, Arrests cell cycle, Induce p53, TSG suppression	Lectins; Quercetin	Tuber, leaves	[20,32,45, 54]

DISCUSSION

As discussed in Table 1, *Aloscasia macrorrhiza* has broad prospects for traditional uses. Due to these uses, the quest to determine the mechanism of action has begun. Giant taro shows anti-microbial action. The antimicrobial activity can be found by analyzing the zone of inhibition, which depends on [37]: The potency shown by the anti-microbial agent and the zone of inhibition differs. The medium on which the compound is used will vary the diameter of the zone of inhibition. Due to the difference in the cell wall layer of Gram-positive and Gram-negative bacteria, the diameter of the zone of inhibition of the same anti-microbial agent in two different cultural media is different. Various components of *Aloscasia macrorrhiza,* which seems to have anti-microbial activity, when compared against standard agents, show a comparative zone of inhibition. Monoterpene and sesquiterpene competitively penetrate the cell walls of bacteria and prevent their cell wall synthesis by inhibiting peptidoglycan synthesis, thus finally arresting the growth of the bacteria. This illustrates the traditional use of *A. macrorrhiza* to treat cuts, wounds, eczema, and abscesses. Therefore, due to the inhibition of the growth of bacteria by preventing their cell wall synthesis, people traditionally used it as an anti-bacterial plant and on wounds to prevent infection.

Different studies show that extracts of *A. macrorrhiza* are a potent antioxidant. The mechanism of antioxidants can be explained by explaining the auto-oxidation mechanism in human mitochondria. The formation of electron donation to form water from oxygen in mitochondria by conversion to superoxide radical, hydrogen peroxide, hydroxyl ion, and finally, water molecule [26,27]. This hydroxyl free radical loses an electron to form water. This protonation is required to reduce the toxic effect of hydroxyl free radicals. Polyphenolic compounds in mitochondria donate hydrogen to these unstable molecules to stabilize them. This prevents further cellular damage, which includes inflammation and lipid peroxidation, by forming an O-O bond in lipids, carcinoma, and tissue injury. Due to an increase in anti-oxidant enzymes and free radical scavenging, this plant reduces oxidative stress. Hence, it prevents the formation of mouth, peptic, piles, and stomach ulcers. Thus, it was used traditionally as a medicinal plant.

Cancer is a very prominent and deadly disease, with huge widespread nowadays. Proto-oncogenes are primarily responsible for the cellular divisions and proliferations under normal conditions. However, genetic mutations in the Proto-oncogenes may result in the formation of Onco genes, which are lethal, resulting in the uncontrolled proliferation of the cancerous cells [51]. Mutations or absences of tumor suppressor genes can also lead to the same fate. Histone modifications and changes are important. In-vitro cell line studies by several researchers show that extracts of Aloscasia macrorrhiza induce apoptosis by increasing the expression of the Tumor Suppressor gene and the p53 protein. Thus, programmed cell death occurs. Lectins and flavonoids are responsible for the extract's anti-angiogenetic effects.

Diabetes Miletus can occur due to impaired secretion of insulin. When the levels of glucose are high in the blood, it triggers the release of insulin from the β-cells present in the islet of Langerhans of the pancreas [42]. The hydroalcoholic extract of the rhizome and stem of *Aloscasia macrorrhiza* has been shown to mimic insulin activity. Also, it induces GLUT-4 receptor opening to reduce the blood glucose level. Alocasin B was shown to increase insulin reaction on the cell surface, which decreases insulin sensitivity. Moreover, the flavonoids act as $\alpha-$glucosidase inhibitor. Due to its blood sugar-managing effect, it was used in traditional medicine to prevent diuresis and infection from wounds and cuts. It was used in Ayurveda to treat Prameha or polyuria, a hallmark of Diabetes.

The tannins present in the *A. macrorrhiza* stem and rhizome can reduce the inflammation in intestinal enterocytes by decreasing the formation of inflammatory mediators like IL-6, IL-2, TNF-α, cytokines, and histamines. This prevents vasodilation and T-lymphocyte recruiting. This prevents multiple contraction and relaxation of intestinal lumen and thus prevent diarrhea. Since it can manage the peristalsis of intestinal lumen, it can even prevent constipation and act as laxative in high amount.

Aloscasia macrorrhiza have several side effects when consumed. Calcium oxalate crystals can often cause local irritation, burning sensation in buccal cavity, oral palate. It might be even allergic to some individual and hence show hypersensitivity reactions.This manuscript encompasses different traditional, ethnomedicinal and Pharmacological importance of *Aloscasia macrorrhiza*. This paper comprises all possible minute details of various research papers, where structural elucidation of different phytoconstituents and their mechanism of action to show Pharmacological effects have been

discussed. This review will enable the future researcher to get detailed knowledge of various aspects of *Aloscasia macrorrhiza* without further searching other Literature. Despite the advancement of technology and pharmacological development, there are still some research gaps. The limitations of phytochemical studies include the lack of a standard extraction method, the variation of phytochemical constituents with geography, and the need for more bioavailability studies. It should be noted that overexploitation and excessive harvesting of giant taro should be avoided for research. Participants in clinical trials for further research should be given consent by an informed consent form.

CONCLUSION

Plants are an immensely important source of medicine, on which more than 80% of people thrive. Due to its immense traditional importance, phytochemical screening of *Aloscasia macrorrhiza* gained importance. Due to different components like Alocasin, this plant species has potent antioxidant, anti-inflammatory, anticancer, anti-fungal, anti-diabetic, anti-microbial, hepatoprotective, and anti-diarrheic effects. This paper will help the researcher understand all researched work and their significant finding on this plant. This paper, being a review work, encompasses only the findings of other researchers. No experimental work has been carried out in our laboratory. Many investigations are yet to be carried out to prepare formulations of phytoconstituents screened from this plant for human use. Proper clinical trials can be carried out to elucidate the dose-related dependence of various hydroalcoholic extracts of different parts of the plant with different diseases. Different doses of different extracts can help streamline the phytoconstituent responsible for the effect and thus can further emphasize the mechanistic approach of the biological effect.

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NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Amitesh Chakraborty and Santanu Giri contributed to idea, data finding, conceptualization, interpretation of findings and writing the original draft and correcting mistakes in the draft; Aditya Dev Shah contributed only to data finding; Tushar Adhikari supervised the findings and reviewed the final draft of writing. All authors have made substantial contributions in preparing the draft of this article. All authors have read and accepted the manuscript.

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