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RESEARCH PAPER

The Medicinal Properties of the Alocasia Genus: A Systematic Review

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Abstract

The objective of this study is to evaluate the existing medicinal studies of the Alocasia genus and identify the possible studies that may be done in the future on its member species. To do this, Science Direct and Google Scholar were used as a database to get the available researches searching for the term "Alocasia" and some of its common species like "Alocasia macrorrhiza". Fifty eight articles were selected and from these, 28 were qualified for this systematic review. Results show that Alocasia species are mostly studied for antioxidant and antitumor and cytotoxic studies and to some extent antimicrobial and glycemic and lipidemic studies which are mostly related to cancer studies. The findings in this study suggest that Alocasia species may be studied further for toxicities and most importantly, cancer ddestudies as based on available literatures, there is a strong pattern that correlates its available medicinal studies to the different stages of cancer development.

1. Introduction

Alocasia genus is composed of tropical plants with mostly showy large leaves. It is generally referred to as Elephant's ear for this reason [1]. While mostly used as ornamental, there is a potential for medicinal use among its species as can be seen in this exhaustive systematic review on its medicinal property where drug discovery studies are slowly becoming popular for the genus. There are also new species that are discovered from time to time giving the opportunity to study novel molecule like the following species: *Alocasia nycteris* in the Philippines [2], *Alocasia hypnosa* in China [3], and those in Thailand like *Alocasia hypoleuca*, *Alocasia longiloba*, *Alocasia navicularis* and *Alocasia perakensis* [4].

Alocasia species has also been known as vegetable apart from its ornamental purpose and medicinal properties like *Alocasia indica* (Roxb.) Schott [5]. As mentioned, Alocasia grows in countries with tropical climate and there are ethnopharmaceutical practices in most of these countries brought about by the natives that may provide a good clue and guidance in studying the genus. Like the use of *Alocasia macrorrhiza* (Linn.) in cough and toothache [6] and as antimalarial [7] and *Alocasia indica* (Roxb.) Schott for abscess [8] and as a nyctalopic [9], these are few of the folkloric uses of the plants in the genus. Studying the plant onwards drug discovery is very important as a lot of species remain unexplored for medicinal purpose like the endemic *Alocasia sanderiana* Bull. in the Philippines that have limited researches.

2. Methodology

The word "Alocasia" was searched under Google Scholar and Science Direct and a total of 58 articles were retrieved last mid-June of 2016. Out of the 58 articles, 9 were not included due to non-medicinal topics about Alocasia like biotechnology, farming and chemical studies. Another 9 articles were excluded due to taxonomical, ethnopharmaceutical and nutraceutical nature and were instead used as supplemental to this review. Ten articles were finally excluded because they only discuss Alocasia in part and not as the main topic of the study, these studies were also used as a supplemental to this article instead. A total of 28 articles were used for this systematic review that may add knowledge to the medicinal use of the Alocasia genus.

3. Results

There are very few medicinal studies done on Alocasia genus most of which are on antioxidant property and antitumor and cytotoxic studies. Below is the exhaustive literature review on the medicinal studies of the Alocasia genus and Table 1 summarizes its medicinal property per species.

3.1. Antimicrobial Studies

Among the antibacterial studies of Alocasia genus is that of Saswati et al [10], were *Alocasia decipiens* Schott rhizome (roots) methanolic extract gave a 16 mm zone of inhibition against *Staphylococcus aureus* using the 100% concentration of the extract in a modified filter paper disc diffusion method with different antibiotic comparisons, this is consistent to the methanolic extract that gave a 1 mm zone of inhibition in the study of Ongpoy [11] moreover with bigger zones using the dichloromethane fraction at 4 mm with *Proteus mirabilis*, 3 mm with *Pseudomonas aeruginosa* and 1 mm with *Pectobacterium carotovorum* using the disc diffusion method without antibiotic comparison but this time with *Alocasia sanderiana* Bull. leaves. in the study of Islam et al [12], disk diffusion method was also employed using *Alocasia indica* (Roxb.) Schott tuber, this study also gave a moderate zone of inhibition that ranges from 5.8 to 9.8 mm for gram positive and 12.1 mm to 18 mm for gram negative at 250 and 500 ug/disc, the organisms tested were *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Salmonella typhi*, *Shigella flexneri*, *Shigella sonnei* and *Shigella dysentery*. Using *Alocasia fornicata* leaves and stolons (roots) in the study of Hague et al [13], the chloroform, ethyl acetate and ethanolic extracts of the said plant gave moderate-to-good antimicrobial activity with an average zone of inhibition at 8-20 mm.

For antifungal studies, it has been identified that Alocasin, may be the antifungal present in the rhizomes of *Alocasia macrorrhiza* as isolated by Wang et al [14] which may justify the same antifungal activity in *Alocasia odora* methanolic extract using its leaf, rhizome and leafstalk as reported by Wang et al [15] which gave an overall 89.12% inhibition using the trichloromethane extract at 10 mg/mL against various fungal specimens.

3.2. Antioxidant Studies

Antioxidant property is one of the most studied Alocasia medicinal use. Among the Alocasia genus, *Alocasia indica* (Roxb.) Schott is the mostly utilized for antioxidant property. Patil et al [16] found significant free radical scavenging activity in the ethyl acetate and n-butanol fractions of the plant using DPPH (1, 1-Diphenyl-2-Picryl-Hydrazyl), superoxide anion radical and nitric oxide tests which may be due to the presence of phenol in its root although in this study IC_{50} results were not shown and discussed but was present in the method, it would have been a good quantitative evidence of inhibition to oxidation. Another study from Islam et al [12] showed strong radical scavenging activity using its tuber which may be again due to phenol content and on top of this, flavonoid using DPPH test. This study though seems to address less of antioxidant due to the many pharmacologic activity that it seems to include compromising detail and quality of the work. In a much more comprehensive study from Pal et al [17], DPPH, hydroxyl, nitric oxide and superoxide tests were employed in the plants ethanolic fraction using its tuber as well that eventually gave a positive result. Tubers though are not the only plant organ studied for antioxidant using *Alocasia indica* (Roxb.) Schott, in the study of Mulla et al [18] the hydroalcoholic extract of the plant leaves also possess potent antioxidant activity that may be attributed to the presence of flavonoid using DPPH, nitric oxide and hydroxyl radical tests.

There are also studies for *Alocasia macrorrhiza* on its antioxidant properties, one is from Patil

et al [19] where activity was found to be present utilizing TBARS (Thiobarbituric Acid Reactive Substances) and glutathione tests in which the plant leaves were used. Rahman et al [20] further explored the IC_{50} value of the plant which is 693 ug/mL using DPPH test of the rhizome. The ground parts were later on found to have more antioxidant activity than the aerial parts of the plant using solvent fractions of hexane, benzene, toluene, chloroform, diethyl ether, ethyl acetate and water still using DPPH in the study of Mandal et al [21] who also studied *Alocasia fonicata* with the same findings. There is also a study on *Alocasia decipiens* Schott rhizome using its methanolic extract tested through DPPH and FRAP (Ferric Reducing Antioxidant Power) from Saswati et al [22] that identified IC_{50} of 14.78 $\pm$ 0.95 ug/mL which may be due to its phenol and flavonoid contents.

3.3. Glycemic and Lipidemic Studies

There are few studies on the Alocasia genus that deals with antidiabetic and antihyperlipidemic. Jawaid et al [23] found out that there is significant decrease in blood glucose level as well as a significant decrease in serum total cholesterol, triglycerides, LDL, VLDL, and increase in HDL in a study using *Alocasia indica* (Roxb.) Schott rhizomes where rats are induced with lipidemia and type 2 diabetes through High Fat Diet/Streptozotocin (HFD/STZ) and Streptozotocin/Nicotinamide (STZ/Nicotinamide). In these 2 group treatments, methanolic extract were induced at 100-200 mg/kg body weight that lasted for 28 days using HFD/STZ while 15 days for STZ/Nicotinamide with glibenclamide as the control. The study did not give any correlation though between the HFD/STZ and HFD/Nicotinamide groups.

In the study of Rahman et al [20] using *Alocasia macrorrhiza* (Linn.) rhizome, methanolic extract was used in alloxan-induced hyperglycemic mice at 250 mg/kg and 500 mg/kg were the 500 mg/kg produced decrease in glucose level significantly compared to metformin. *Alocasia indica* (Roxb.) Schott was again used in the study of Patil et al [24] but this time leaves were utilized instead of roots to STZ induced diabetic rats at 200 m/kg and 400 mg/kg body weight doses also using glibenclamide. Results show that there is decrease in blood glucose level and serum lipid profiles which are cholesterol and triglyceride in the test animals which may confirm its traditional use to manage lipidemia and diabetes.

3.4. Antitumor and Cytotoxic Studies

Alocasia cucullata (Lour.) G. Don and *Alocasia macrorrhiza* (Linn.) has been studied for antitumor property. *Alocasia cucullata* (Lour.) G. Don tubers show potent antitumor activity both *in vivo* and *in vitro* in a study conducted by Wei et al [25] where in its *in vivo* study, the cancer expression was down regulated at p-Akt and p-ERK while upregulating Bax/BCl-2 ratio and caspase 317 activation and in its *in vitro* study, antiproliferation of G_0/G_1 phases and cell apoptosis. This study used MTT assay on 5 cell lines to possibly decode the mechanism of action of gastric cancer inhibition previously discussed of the plant using butanol, petroleum ether, ethanol and water fractions of the plant confirming its traditional Chinese medicinal use for cancer.

Alocasia cucullata (Lour.) G. Don roots was further studied by Peng et al [26] using a total of 50 male mice studied for immune response and survival measurement where increase in cytokines by the plant may induce antitumor activity, cytokines such as IL-2, IFN-γ and TNF-α. The plant also induce THP-a differentiation into macrophage cell. In survival measurement 43 days is the mean, giving 16 days longer than the control group is noted from the test mice which may also further explain the said use in Chinese medicine for cancer.

Alocasia macrorrhiza (Linn.) was also studied *in vivo* using MTT assay by Zhao [27] where a good cytotoxicity was observed in ethyl acetate and acetone fractions against A549, B16, BGC-823 and NG 108-15 tumor cells. *In vitro* studies on the plant was also done by Ke et al [28] but there is generally no antitumor effect that is evident.

There were also cytotoxicity studies conducted for Alocasia genus but all of which are based on an old method of brine shrimp lethality test. In the study of Rahman et al [20] 188.14 ug/mL was found to be the LC50 of *Alocasia macrorrhiza* (Linn.) rhizome, Islam et al [12] declared 81.09 ug/mL LC50 of *Alocasia indica*

(Roxb.) Schott tuber and for Hague et al [13] who studied the chloroform extract of the leaf, ethyl acetate extract of the stolon and another ethanol extract of the stolon showed LC50 of 13.98 ug/mL, 12.26 ug/mL and 12.81 ug/mL respectively.

Table 1: Studies on the Medicinal Properties of the Alocasia Species

Alocasia Species	Medicinal Property	Plant Organ Used	Author & Date Published
Alocasia cucullata (Lour.) G. Don	Antitumor	Tubers (Stems)	Wei et al, 2015
	Antitumor	Roots	Peng et al, 2013
Alocasia decipiens Schott	Antibacterial	Rhizome (Roots)	Saswati et al, 2013
	Antioxidant	Rhizome (Roots)	Saswati et al, 2013
Alocasia denudata Engler	Wound healing		Abdul Latif et al,
Alocasia fornicata	Antibacterial	Leaves and Stolons (Roots)	Hague et al, 2014
	Antioxidant	Leaves; Rhizomes & Stolons (Roots)	Mandal et al, 2010
Alocasia indica (Roxb.) Schott	Antibacterial	Tuber (Stems)	Islam et al, 2013
	Antioxidant	Roots	Patil et al, 2012
	Antioxidant	Tuber (Roots)	Islam et al, 2013
	Antioxidant	Tuber (Roots)	Pal et al, (not indicated)
	Antioxidant	Leaves	Mulla et al, 2009
	Antidiabetic	Rhizome (Roots)	Jawaid et al, 2015
	Antihyperlipidemic	Rhizome (Roots)	Jawaid et al, 2015
	Antidiabetic	Leaves & Stems	Karim et al, 2014
	Antihyperlipidemic	Leaves	Patil et al, 2012
	Hepatoprotective	Tuber (Stems)	Pal et al, 2014
	Hepatoprotective	Tuber (Stems)	Pal et al, (not indicated)
	Hepatoprotective	Leaves	Mulla et al, 2009
	Anti-inflammatory	Rhizome (Roots)	Rahman et al, 2011
	Analgesic	Rhizome (Roots)	Rahman et al, 2011
	Anti-diarrheal	Tuber (Stems)	Islam et al, 2013
	Anti-diarrheal	Leaves	Mulla et al, 2011
	Anthelmintic	Leaves	Mulla et al, 2010
	Anthelmintic	Roots	Patil et al, 2012
Alocasia macrorrhiza Linn.	Antifungal		Wang et al,
	Antioxidant	Leaves; Rhizomes & Stolons (Roots)	Mandal et al, 2010
	Antioxidant	Rhizome (Roots)	Rahman et al, 2012
	Antidiabetic	Rhizome (Roots)	Rahman et al, 2012
	Antitumor	(not indicated)	Zhao, 2008
	Hepatoprotective	Leaves	Patil et al, 2011
	Anticancer	(not indicated)	Fang et al, 2012

Alocasia odora	Antifungal	Leafage and Leafstalk (Leaves) & Rhizomes (Roots)	Wang et al, 2006
	Wound healing	Stems	Viet et al, 2006
Alocasia sanderiana Bull.	Antibacterial	Leaves	Ongpoy, 2015

3.5. Hepatoprotective Studies

Alocasia indica (Roxb.) Schott has the most liver studies. Pal et al [29] studied the hepatotoxicity reduction of the ethanolic *Alocasia indica* (Roxb.) Schott extract from the plant tuber where 200 mg/kg and 400 mg/kg body weight per day for 15 days were administered to test rats with alcohol induced liver damage. Upon histopathlogic evaluation, hepatic cell architechture was preserved moreover when antioxidant tests were employed, hepatic catalase and superoxide dismutase were restored to normal. Another study from the same group of Pal et al [17] utilizing the same plant organ used albino wistar rats with CCl_4 induced liver damage, result showed that there is hepatoprotective activity especially in the ethanolic extract administered at 200 mg/kg for 7 days. In the same study, presence of phytosterols, alkaloids, flavonoids, glycosides, saponins and tannins were revealed using PerkinElmer GCMS. Phytochemical testing was also conducted were flavonoids and phenols are found to be more concentrated in ethanolic extracts. Mulla et al [30] used 250 mg/kg and 500 mg/kg body weight of hydroalcoholic extract of the same plant to CCl_4 and paracetamol liver damaged rats were hepatic steatosis, fatty infiltration, hydropic degeneration and necrosis were not present in animals administered with the extracts.

There are also studies using *Alocasia macrorhiza* (Linn.) where leaves are used as hepatoprotective agent in rats with CCl_4 and tylenol induced liver injury. In this study of Patil et al (10) where the plant decreased the leakage of AST (Aspartic Amino Transferase), ALT (Alanine Amino Transferase) and ALP (Alkaline Phosphatase) in an *in vitro* study utilizing the liver slice method confirming the presence of hepatoprotection. Although a laboratory paracetamol USP grade should have been used instead of the commercial Tylenol. Fang et al [31] also studied *Alocasia macrorrhiza* (Linn.) to confirm its anticancer activity using different cell lines that later showed inhibition in hepatoma growth.

3.6. Anti-inflammatory and Analgesic Studies

Rahman et al [32] studied the *Alocasia indica* (Roxb.) Schott ethanolic extract of dried rhizome for analgesic and anti-inflammatory properties. For the analgesic test, significant writhing inhibition in acetic acid-induced writhing was observed using mice which is comparable to that of diclofenac sodium. The dose administered was 25 mg/kg body weight for the anti-inflammatory test, carrageenan-induced paw edema shows significant result comparable to aspirin at dose of 150 mg/kg body weight. This results support the use of the plant traditionally in Bangladesh for inflammation. However the extraction procedure used 1:4 other than the standard 1:10 ratio of plant material to solvent and the use of animals in analgesic is too much at 10 and too little at 6 for anti-inflammatory.

3.7. Antidiarrheal Studies

The tuber of *Alocasia indica* (Roxb.) Schott was studied *in vivo* for antidiarrheal property using mice induced with castor oil diarrhea and another group with magnesium sulfate induced diarrhea. This study from Islam et al [12] showed significantly decreased defecation including the latent period of defecation for both procedures at 250 mg/kg and 500 mg/kg body weight using ethanolic extract. The studies for antidiarrheal property for Alocasia genus seem weak though like the other one from Mulla et al [33] were *Alocasia indica* (Roxb) Schott was also used in aqueous and ethanolic extracts showing *in vitro* antidiarrheal activity.

3.8. Anthelmintic Studies

There are 2 anthelmintic studies for Alocasia genus both for *Alocasia indica* (Roxb) Schott. A study from Mulla et al [34] used 3 fractions of its leaves, hydroalcoholic, petroleum ether and ethyl acetate against the earthworm, *Pheretima posthuma* with extract concentrations at 10, 25 and 50 mg/mL suspended each in 40 mL formulations using piperazine citrate as the standard drug. It was

found out that the hydroalcoholic extract was more effective at 50 mg/mL but all extracts were vermifuge and vermicidal. This study used an earthworm instead of a human helminth because of its strong resemblance and availability.

The other study is from Patil et al [35] where alcoholic and ethyl acetate fractions were used comparing it to albendazole as the standard drug and *Pheretima posthuma* as the test organism. The study is consistent to the previous study discussed where significant activity that is paralysis and death of the test organism resulted which may be due to the presence of flavonoid and phenolic compounds.

3.9. Wound Healing Studies

*Alocasia o*dora (Roxb.) Koch and *Alocasia denudata* Engeler has been tested for wound healing activities. Based on the study of Viet et al [36] where skin fibroblast proliferation assay-guided fractionation was used combined with instrumental and biochemical techniques confirmed the Vietnam wars use of the plant as wound treatment through the proliferation of skin fibroblast shown in the research. In the study of Abdul Latif et al [37] where a total of 120 wistar rats were used for the test using the stem juice of *Alocasia denudata* Engler compared to the 10% solcoseryl gel, wounds treated with *Alocasia denudata* Engler possess a significant rate of wound contraction with organized epithelial layer with dense and compact collagen fibers that supports its traditional use for wound healing.

Discussion

Alocasia genus are indeed good plants to explore for medicinal properties as there are so much unexplored indications and constituents to discover. It is also important to note that while medicinal properties may be seen with the genus there are also toxicity studies that should be given attention. One is the recorded 55 cases of plant poisoning at the Milan Poison Control Center [38] brought about by the Alocasia genus, another is the reported case were 2 patients experienced oral numbness and intractable tongue pain with one of these patients suffering from upper respiratory tract obstruction after ingesting raw *Alocasia odora* [39]. Neurotoxicity brought about by the sapotoxin in the tuber of *Alocasia macrorrhiza* (Linn.) [40] has also been reported and lastly the fatal food poisoning following ingestion of its fruit with manifestations that are the same as that of cyanogenic glycoside poisoning [41]. This poisoning may be brought about by the presence of plant raphide crystals [42] that causes irritation and has also been reported for *Alocasia odora*, *Alocasia indica* (Roxb.) Schott [43] and *Alocasia sanderiana* Bull. [11]. in the form of calcium oxalate. Another reported toxic compound may be the lectin of *Alocasia macrorrhiza* (Linn.) which has been said to be toxic to insects [44] although there are also recommended veterinary antidote for Alocasia species poisoning which are sodium thiosulfate and sodium nitrite [45]. Some natives though try to remove the poison as it is an important food for them [46]. On the contrary, there is also a study that mentioned the use of Alocasia against snake venom [47]. therefore toxicity is also an area that needs to be explored.

It is also good to note that based on this systematic review, there is a good opportunity for studying chemoprevention. The antioxidant studies are proof that Alocasia genus may prevent a number of human diseases including cancer [48]. The anti-inflammatory studies on the other hand support the need for chemopreventive studies as inflammation supports the different stages of cancer formation which are initiation, progression and promotion [49] [50]. Some forms of cancer may also be caused by microorganisms [50] like *Helicobacter pylori* in the GIT in which Alocasia has been shown to have antimicrobial properties. Most importantly, the 4 hepatoprotective studies on Alocasia genus are used against cancer based on this review. Therefore a pattern of chemopreventive opportunity may be seen based on this trend and should be given more attention for future studies on other species like *Alocasia sanderiana* Bull. especially with the recent taxonomic developments in the Philippines for the genus [51]. Indeed, the Alocasia genus is promising and more studies should be seen in the next years owing to its potential for medicinal purposes from this review.

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Competing Interest

The author declares that he is an employee of PerkinElmer in the Philippines, in which one of the instruments in the articles reviewed is from

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