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CURRENT HIGHLIGHTS ON BIOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *DIOSCOREA ALATA* : A REVIEW

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ABSTRACT

Dioscorea alata, also known as water yam is an important plant found globally. Nearly 600 different yam species have been reported around the world. *D. alata* is an edible product, it is highly cultivated in countries like tropical South America, Africa, Australia, and South-eastern U.S. *Dioscorea alata*, commonly known as water yam, purple yam, ube, or greater yam has been reported to have diverse activities in various diseases. *D. alata* belongs to dioscoreaceae family and has been found to have antioxidant and anti- inflammatory, anti-apoptotic properties. The metabolic products of *dioscorea alata* are phenolic compounds, reducing sugars, flavonoids, glycoside, saponins, alkaloids, anthraquinones, proteins, tannins etc. The active constituents of *D. alata* are diosgenin, dioscorine, dioscin, cholin, mucin, allantoin, crude fat, crude fiber, catechins, chlorogenic acids, proanthocyanidins, myricetin, diosbulbin and sapogenin. Diosgenin is one of the main steroidal glycoside has been reported to have different activities like anti-diabetic activity, anti-hypertensive activity, anti-cancer activity, anti-inflammatory activity and cardio protective activity. Diosgenin is effective in heart disease due to the anti-oxidative and anti-apoptotic activity. Diosgenin has also been found to reduce oxidative stress and increase the levels of glutathione, SOD and catalase activity. Diosgenin also reported to inhibit the apoptosis by reducing the activation of caspase 9, a pro-apoptotic factor. Furthermore, bioactive compounds, including diosgenin, anthocyanins and dietary fiber of *D. alata* tuber has potential to prevent the condition of hyperlipidemia by normalizing blood lipid profiles. However, further investigations are required to find the effect of *D. alata* on cardiovascular disorders.

Keywords: *Dioscorea alata,* Diosgenin, Anti-oxidant.

Introduction

Dioscorea alata is an herbal plant found naturally in various area of the world such as tropical area, Africa, Australia. This plant also available in North America, Japan, China, Mexico, India and Nepal. *D. alata* is a yam species is grown worldwide. Around the world, approximately 600 different yam species are grown. The common names of *D. alata* are Kath Alu, Banra, Bahra, also named as water yam, purple yam, ube, or greater yam (Rao and George, 1990). The stems of *D. alata* are purplish winged with long petioled, leaves are bright green color and flowers are yellow-white. *Dioscora alata* is an annual and perennial climbing plant. *D. alata* is a principle source of nutrition (Baah *et al*., 2009). The tubers of the plant are cylindrical, tuber flesh is white in color and texture is watery. The height of this plant is 20-30 feet, it is a seasonal plant, and tubers are violet-purple to bright lavender in color. The different active constituents of *D. alata* are diosgenin, dioscorine, dioscin, cholin, mucin, allantoin, crude fat, crude fiber, catechins, chlorogenic acids, proanthocyanidins, myricetin, diosbulbin and sapogenin. *D. alata* also contains glycoside, flavonoids, alkaloids, tannins, triterpenes, coumarins, phytosterols, steroids etc (Dumont and Vernier, 2000; Dutta, 2015). The inorganic constituents present on tubers of *D. alata* are Vitamin A_1, Vitamin C, Ca, K, Co, Fe, Mg, Mn, vitamin B_3, PO_4, Vitamin B_2 & B_1, Se, Si, Na, Sn, Zn (Dumont and Vernier, 2000; Mishra *et al.,* 2008). A number of pharmacological activities of *D. alata* such as anti-diabetic, anti-hypertensive, anti-oxidant and anti-apoptotic activity, anti-infective, anti-cancer, anti-microbial, cardio protective, hypolipidemic, hypo-cholesteric activity have been reported and are mainly due to the presence of chemical substances diosgenin present in its tissue (Mulualem *et al*., 2018). Diosgenin is a best active constituents of *Dioscorea alata* having anti-oxidant activity. Various studies have revealed the protective effect of antioxidants on heart as these agents protect myocardium against ischemia reperfusion injury. Other natural antioxidants dioscin and dioscorin found in *Dioscorea alata,* can also protect cells from oxidative stress by preventing the formation of ROS (Kumar *et al*., 2017).

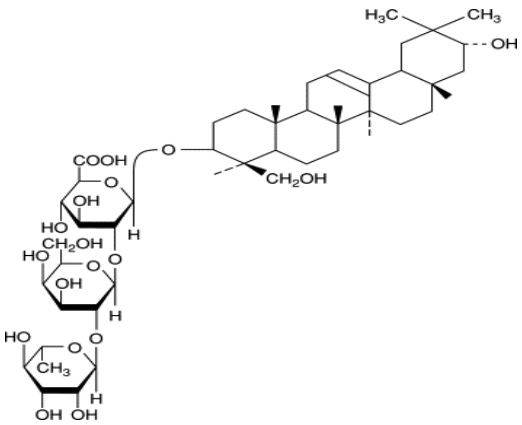

Fig 1: Steroidal saponin

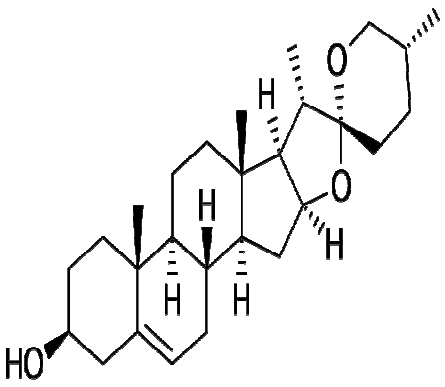

Fig 3: Steroidal diosgenin

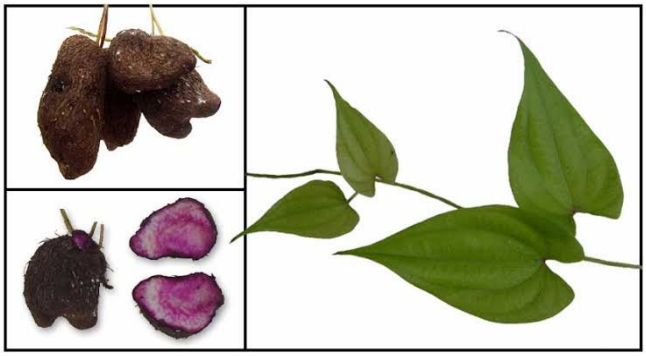

Fig 2: *Dioscorea alata* leaves and tubers.

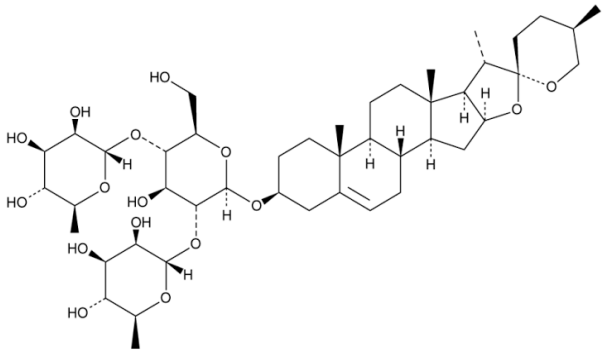

Fig 4: Dioscin

Pharmacological activities of *Dioscorea alata*

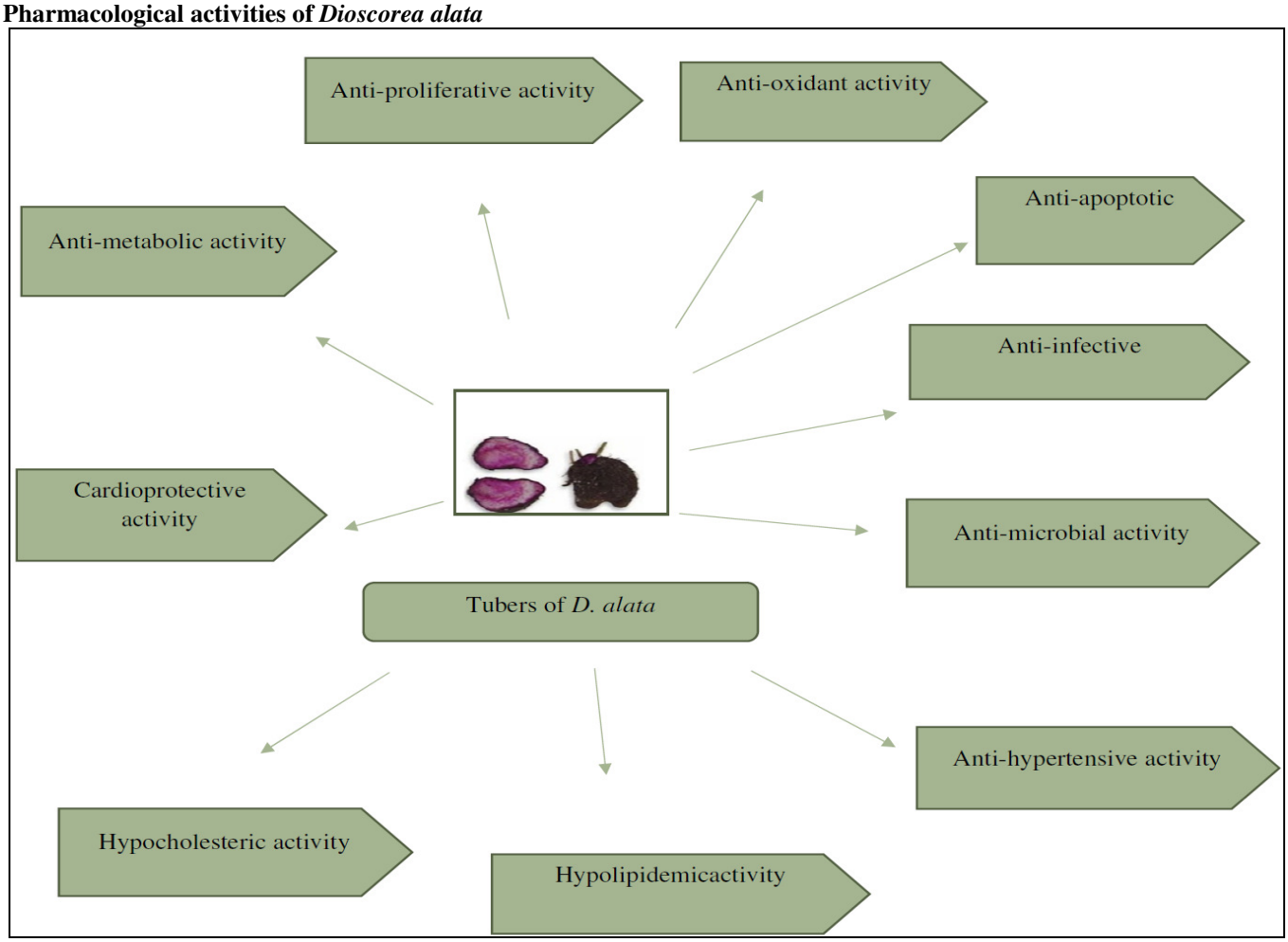

Fig 5: Pharmacological activities of *D. alata*

Distribution

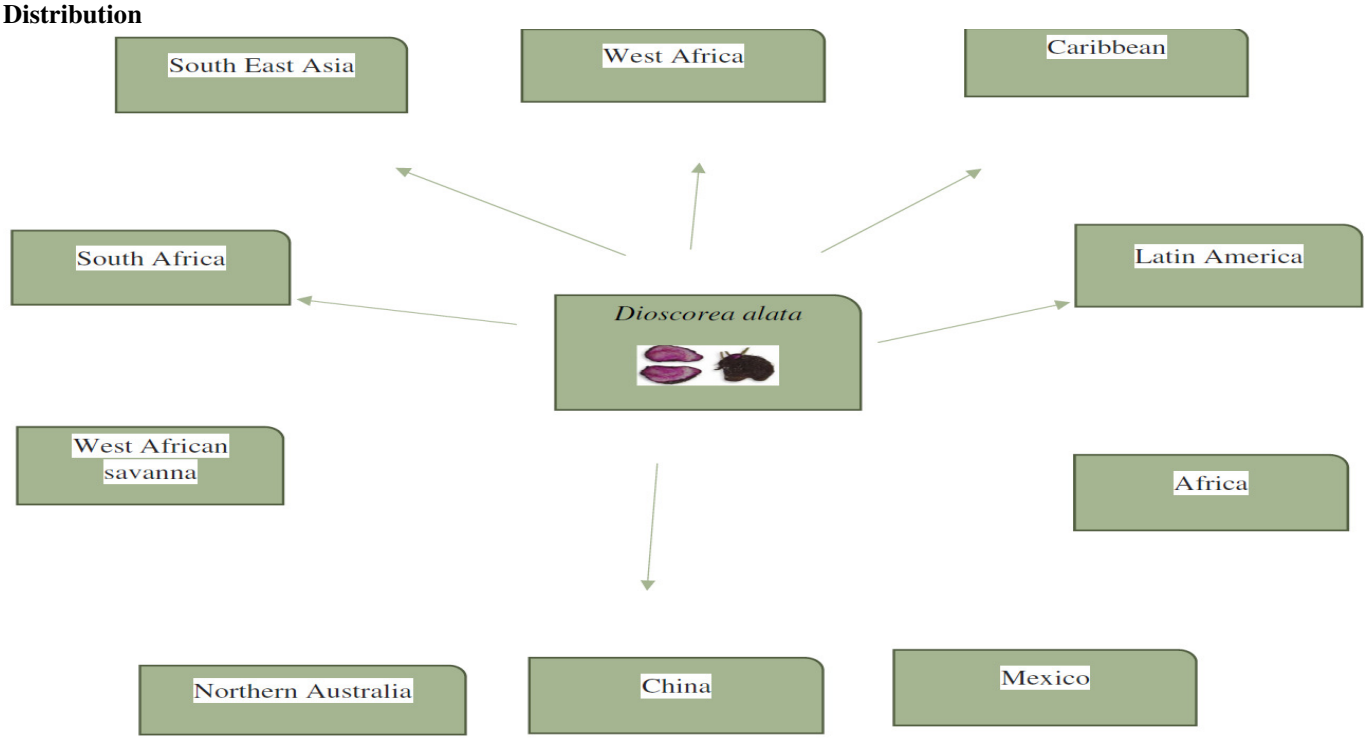

Fig 6: Distribution of *Dioscorea* species around the world

List of *Dioscorea* species and their origin

Yam species	Scientific name	Common Name	Habitat	Medicinal uses	Origin
Greater yam	*D. alata* (Dutta, 2015; Wanasundera and Ravindran, 1994)	Kath Alu (As), Banra (HR), Bahra (HM), Kham Alu (Beng)	Climber	Cure piles, kill stomach worm, anti-diarrheal, anti-inflammatory, anti-diabetic, anti-cancer, anti-hypertensive, hypolipidemicand hypo cholesteric.	South East Asia
Yellow guinea yam	*D. cyanensis* (Dumont and Vernier, 2000)	Affoo (Spanish), Igname blanc (French), Huangshuyu (Chinese)	Vine/ climber	Cardio protective, anti- diabetic, steroidal drug.	West African forest
White/ African yam	*D. rotundata* (Mbiantcha *et al*., 2011)	Ighnam	Climber	Anti-diarrheal, anti-inflammatory.	West African savanna
Cush cush yam	*D. trifida* (Mollica et al., 2013, Pérez *et al.,* 2011)	Mapuey (Venezuela), Inhame (Brazil)	Climber	Laxatives, anti-emetics, arthritis, anti-inflammatory, contraceptives and gene amplification.	Tropical America
Aerial yam	*D. bulbifera (*Adesanya *et al*., 1989; Mbiantcha *et al.,* 2011*)*	Mas alu, ruipan, gosh alu.	Climber	Appetite stimulant, dysmenorrhea, rheumatoid arthritis, antacids, spasmodic asthma, labor pain, hernia, skin infections, reduce throat pain.	Latin America
Intoxicating yam	*D. hispida* (Hgaza *et al.*, 1989)	Hati-muriaalu (As.), Thadangjia (DI).	Creeper/Climber	Fish poison, vomiting, indigestion, purgative, wounds and injuries.	Southeast Asia
Five leaf yam	*D. pentaphylla* (Poornima and Ravishankar; 2007; Hamburger *et al*., 1989)	PaspotiaAlu (As.), Thaphin (DI), Ram bahra (HM), Baha (MI), Ruipheng (Karbi)	Climber	Skin infections, rheumatoid arthritis, anti-fungal and anti-ulcer.	Northern Australia
Bitter yam	*D. dumetorum* (Mustafa *et al*., 2018)	Three-leaved yam	Vine/herbs	Arrow poison, jaundice.	Africa
Nepal yam	D. deltoid (Dutta, 2015)	Kukurtarul (Nepali)	Climber	Synthesis of steroidal drugs,	Latin America
Dioscorea Yam	*D. composite* (Dutta, 2015)	barbasco	Climber	Oral Contraceptives, arthritis, diabetic neuropathy.	Mexico
Yucca elephantipes	*D. elephantipes* (Zhang *et al*., 2008)	Elephant's foot yam	Vine/climber	Oral contraceptives, anti-diabetics, anti-inflammatory activity.	South Africa
Yam	D. zingiberensis (Huang *et al*., 2008)	Tuberous root vegetable	Vine/climber	Cardio protective, steroidal hormone synthesis, hyperlipidemia, neuroprotection.	China

Lesser yam	D. esculenta (Ravindran and Wanasundera; 1993)	Moa Alu (As), Ruipheng silu (Karbi).	Climbing shrub	Alimentary disorders, throat pain, chest pain, nervous disorders and swellings.	Southeast Asia
Yam	*Dioscorea pubera* (Dutta, 2015)	Ruichelong (Karbi)	Climber	Cure colic pain, appetite stimulantsand anti-emetics.	Idukki, Wayanad
Yam	*Dioscorea sativa* (Mbiantcha *et al.,* 2011*)*	Kath Alu (As.)	Climber	Skin infection, stomach pain and steroidal drug synthesis.	Tropical area
staple yams	*Dioscorea arachnida* (Zhang *et al*., 2008)	Tinipotia alu (As.), Ruisanglang (DI	Climber	Tubers are boiled or roasted and occasionally used in curries	Northeast Indian
Chinese yam	*Dioscorea oppositifolia* (Poornima and Ravishankar; 2007)	Not known	Climber	Antiseptic for ulcers, epilepsy.	Myanmar
	Dioscorea hamiltonii (Mustafa *et al*., 2018)	Ban-tarul (Nepali), Ruikaulang (Karbi)	Climber	Tubers are used to cure dysentery.	China
Wild Yam	*Dioscorea villosa* (Wojcikowski *et al*., 2008)	Thapu–nairo (DI)	Climber	Antispasmodic, coughs, hiccoughs,rheumatoid arthritis,muscular spasms, croup and gas.	Eastern North America
Yam	*Dioscorea aculeate* (Mustafa *et al*., 2018)	Thagdi (DI), Barhtlum (HM)	Climber	Tubers are boiled and also used as vegetable for its sweet taste.	Prain and Burkill
Yam	*Dioscorea bellophylla* (Mitchell *et al*., 1995)	Ruiding (Karbi).	Climber	Treat fever, malaria, headache, and dysentery and lowers blood cholesterol.	Arunachal Pradesh

Cultivation of *Dioscorea* species

Soil and climate

Dioscorea alata is a perennial plant and can grow in any type of soil, however, its maximum growth occurs in warm, humid land, in light and deep loam soils (Hgaza *et al*., 2011). The optimum pH required for maximum growth is 6.2 to 7 i.e. neutral. Soil should be well drained for better growth of plant but sometimes it can also grow in drought conditions regardless of water requirements (Paramjeet *et al*., 2018).

Rainy season is the best for dioscorea spp cultivation, therefore, May to August are the prime months for cultivation of *Dioscorea alata.* The piece of tubers or mature tubers from previous crop can be seeded in soil. The roots of the *Dioscorea alata* are capable to produce new plant (Malapa *et al*., 2008). The temperature required for the growth of *dioscorea* spp is 25 °C to 30 °C. Time required for the formation of tubers is 8 to 9 months (Malaurie *et al*., 1995). Organic matter is added to the cultivated land which prevent soil damage, irrigation of soil is also required that increases the microbial activity of the soil (Mignouna *et al*., 2009). Watering the plants at least once a week is required. Harvesting is done after 9 to 10 month when *Dioscorea alata* becomes fully matured (Hochu *et al*., 2006).

Phyto-chemistry

Dioscorea alata contains a number of phytochemicals present in its various parts and reported to possess potential biological properties. The bitter and unpleasant taste of *Dioscorea alata* tubers is due to diosbulbins A & B and dioscorin which causes the toxicity to nervous system and also causes vomiting and diarrhea (Wanasundera *et al*., 1994; Devarkar and Bhogaonkar, 2014).

The major constituent of *Dioscorea alata* is diosgenin have shown to possess a number of pharmacological activity like anti-diabetic activity, anti-hypertensive activity, anti-cancer activity, anti-inflammatory activity and cardio protective activity (Chang *et al*., 2005). Diosgenin is effective in heart disease due to the anti-oxidative and anti-apoptotic activity. *Dioscorea alata* also contains dioscorine, dioscin, cholin, mucin, allantoin, crude fat, crude fiber, dietary fibre (7%), sugars (5.7), protein (6.0%), amylase (29.5), catechins, chlorogenic acids, proanthocyanidins, myricetin, diosbulbin and sapogenin. Inorganic materials present on the tubers of *Dioscorea alata* are A_l, Vitamin C, Ca, K, Co, Fe, Mg, Mn, vitamin B_3, PO4, Vitamin B_2 & B_1, Se, Si, Na, Sn and Zn (Jesus *et al*., 2016; Sheikh *et al*., 2009). The bioactive materials present in *Dioscorea alata* are glycoside, flavonoids, alkaloids, tannins, triterpenes, coumarins, phytosterols and steroids etc. (Zhang *et al*., 2008; Poornima *et al*., 2007).

The active substances present on *Dioscorea alata* tubers are effective in reducing cholesterol level by acting through the HMG-CoA reductase pathway (Chang *et al*., 2005). Diosgenin is effective in reducing inflammation by acting through reducing the inflammatory mediators like TNF-α, LT, IL-6 and AST & ALT. Diosgenin reduces oxidative stress and increases the level of glutathione, SOD and catalase activity, therefore, found to be efficacious as antioxidant and anti-apoptopic in heart diseases (Hgaza *et al*., 1989). Diosgenin also reported to inhibit the apoptosis by inhibiting the activation of caspase 9, a pro-apoptotic factor.

Pharmacological application of *D. alata* in different diseases

Cardiovascular disease

WHO reported that 17.9 million people death occurs due to CVDs in 2016 globally. Various diseased conditions are responsible to cause heart disease such as hypertension, diabetes as well as hyperlipidemia. Males are more prone to heart attack than females. Mostly people of low income countries are affected more. Furthermore, from 2017 report, WHO mentioned that 31% global deaths occur due to heart disease. In England around 34% death due to Coronary vascular disease, in Europe around 40% deaths due to CVDs. Currently, 80% mortality in developing countries reported to be due to CHD, it is expected that CVDs will be major cause of deaths by 2020 (Stewart *et al*., 2017). The risk factors associated with CVDs are smoking, alcohol consumption, diabetes, high blood pressure, high cholesterol level, junk food, atherosclerosis etc. From US data, it was found that 30% of deaths rate in US due to smoking. Cessation of

smoking is the most effective treatment in controlling CAD. For reducing the risk of heart diseases, patients should concentrates on the food habits, exercise (McMullen *et al*., 2018) and blood pressure and on lipid profile (Yan *et al*., 2015). Stress is the hall mark of cardiovascular diseases (Stewart *et al*., 2017). Empirically developed dietary inflammatory potential (EDIP) is associated with obesity, a cardio metabolic risk factors. EDIP can be used for identification of cardiovascular disease risk factors (Farhangi *et al*., 2018). The ethanol and water extract of *D. purpurea, D. japonica* and *D. alata* have been reported to reduce the cardio-toxicity against doxorubicin (DOX)-induced myocardial infarction by reducing the level of TBARS, LDH, ROS and blood pressure (Chen *et al*., 2017; Kim *et al*., 2012). DOX produces oxidative stress, increased blood pressure and activation of caspase 3 which leads to apoptosis. *Dioscorea* extracts are found to be effective in heart disease due to having anti-oxidant, anti-inflammatory and anti-apoptotic activity (Wang *et al*., 2018). Powdered drug of dioscorea rhizome has reduced the oxidative damage in heart and atherosclerosis in hyperlipidemia. Dioscin from the *Dioscorea alata* is also effective in myocardial infarction against streptozocin induced diabetes (Yang *et al*., 2018). Dioscin activates the MAPK pathway and inhibits angiotensin II activation and protect the heart from myocardial hypertrophy (Binesh *et al*., 2018). Diosgenin reduces the inflammatory mediators such as TNF-a, NFkB and COX etc. (Yang *et al*., 2018). Steroidal sapogenin of *D. alata* is effective in myocardial ischemia reperfusion injury.

Inotropic activity

Saponin alter the electrical and mechanical activity of myocardium**.** Saponin also involved in the formation of new blood vessel from pre – existing blood vessel. Saponin also possess vasodilatory activity by stimulating cGMP acting through voltage sensitive Ca2+ channels (McMullen *et al*., 2018). This results into lowering of calcium in the circulation and, therefore, decreases the vasoconstriction due to calcium (Raju *et al*., 2012).

Anti-oxidative activity

Oxidative stress plays an important function in the pathogenesis of various diseases such as neurodegenerative disease like Parkinson's disease, Alzheimer's, dementia and cardiovascular disease such as atherosclerosis, myocardial ischemia and heart attack, inflammatory disease such as arthritis, hepatitis, allergies, inflammatory lung injury and carcinogenesis, metabolic disorder like diabetes mellitus (Mbiantcha *et al*., 2011; Asha and Nair, 2005). Generation of ROS increases the level of TBARS, LDH, CK, MDA and TGF- β1, as well as increase the level of AST & ALT in liver injury. The dioscin present in *D. alata* reduces all the inflammatory parameters and increases the level of SOD, CAT, glutathione and glutathione peroxidase (Sethi *et al*., 2018; Araghiniknam *et al*., 1996). The different types of phytoconstituents found in *D. alata* are saponins, glycosides, flavonoids, tannins, phenols etc. The polyphenol in the form of flavonoids in alata shows good antioxidant activity as it has good free radical scavenging activity (Farombi *et al*., 2000; Ozo *et al*., 1984). The phenolic compounds found in this plant have been reported to have number of biological activities like anti-inflammatory (Ahmed *et al*., 2014), anti-tumor and antimicrobial including anti-oxidant activity (Manivannan *et al*., 2013). The secondary metabolites of the plant *D. alata* are phenolic, alkaloids, saponins, terpenes, lipids, glycosides and carbohydrates (Lubag *et al*., 2008). Aluminum chloride method was used to determine the flavonoids. Steroidal saponin and diosgenin constituents are effective in apoptosis by arresting cell cycle (Moalic *et al*., 2001).

Anti-apoptotic activity

Apoptosis is the programmed cell death, characterized the fragmentation of nuclear DNA and therefore, apoptotic bodies are formed (Dey *et al*., 2016). Macroscopic characteristics of apoptosis is blebbing; bulge of the plasma membrane, plasmolysis, karyorrhexis, karyopyknosis, and apoptotic stimulatory factors such as bid, bak, bax and caspase-3 (Kim *et al*., 2012; Corbiere *et al*., 2003). . The anti-apoptotic factors like bcl-2 family acts against apoptosis and protect the cells from damage. The ethanolic extracts of *dioscorea alata* having protective activity against apoptosis cell death in cardiotoxicity (Tang and Ma, 2011), Dioscin, a constituent of *D. alata* has been reported to decreases the proliferation of cells and acts against the caspase-3 and caspase-9 (Mohan *et al*., 2011; Bhandari *et al*., 2005). Diosgenin also known to protect the cells from apoptosis. The best process to determine the total number of apoptotic cell in apoptosis is tunnel assay. Formalin used as a fixation solution and propidium iodate used as a stain. The viable cells will appears as white and damaged cell appeared as colored (Sakthidevi and Mohan, 2013).

Anti-cancer activity

Diosgenin and dioscin, the main active constituents of *Dioscorea alata*, are effective in several types of cancer. The diosgenin exerts anti-tumor activity through intrinsic mitochondrial apoptosis. Mitochondrial apoptosis occur due to activation of caspase-9, caspase-3 as well as increase in pro-apoptotic proteins such as bak, bax and bid. Diosgenin has been found to reduce pro apoptotic proteins and enhance the activity of anti-apoptotic proteins (Sakthidevi and Mohan, 2013). 70% methanolic extract of D. alata is effective in treatment of cancer and have potential to reduce ROS, as it is a good antioxidant (Asha and Nair, 2005). .

Furthermore, saponins in *D. alata* have outstanding role in destruction of cancerous cells as it interfere with cell division and growth of cancer cell (Bhandari *et al*., 2005; Raju and Mehta, 2008). As cancerous cell is known to possess more cholesterol levels, diosgenin and other alkaloids have been found to have chemoprotective action against cholesterol related inflammation in cancer cells. This chemopretective function is achieved due to alteration of lipid related metabolism in cancer cells (Kanu *et al*., 2018).

Anti-diabetic activity

The diosgenin extracts has been reported to posses anti-diabetic and anti-inflammatory activity (Sangeetha *et al*., 2013). Diabetes characterized by hyperglycaemia, polyuria, polyphagia, weight loss, excessive thirst and blurred vision. The most prevalent complications due to diabetes are retinopathy, neuropathy, and nephropathy as well as atherosclerosis and heart attack. Diosgenin and dioscin reduces related complication due to diabetes (Asha and Nair, 2005). Ethanolic extract of *Dioscorea alata* have significant effect on diabetes mellitus against alloxon-induce diabetes (Maithili *et al*., 2011). Allantoin in *D. alata* also have shown the antidiabetic activity against

streptozocin induced diabetes mellitus (Kim and Park, 2018; Yoon *et al*., 2008). WHO reported that the 90% of the population from developing countries uses traditional drug for primary treatment of diabetes (Akbarzadeh *et al*., 2007).

Anti-hypertensive activity

Hypertension is most common disease in developed as well as developing countries. Dioscorin is one of the chemical constituent of *D. alata* have been reported to have antihypertensive activity (Liu *et al*., 2019). Along with dioscorin, diosgenin is another chemical constituents having anti-hypertensive, anti-inflammatory and anti-oxidant activity (Sakthidevi and Mohan, 2011; Hou *et al*., 2000). Diosgenis is obtained by acidic hydrolysis of glycosides present in *D. alata* have been found to possess vaso-relaxing and anti-hypertensive activity (Kanu *et al*., 2018; Lee *et al*., 2002).

Hyperlipidemic activity

Diosgenin in *D. alata* decreases LDL, triglyceride and total cholesterol and increases good cholesterol HDL (Kanu *et al*., 2018). In one study, the crude diosgenin extracts of *D. alata* tubers have been reported to improve blood lipid profiles (Asha and Nair, 2005). In this study, the purple yam D. alata diosgenin crude extract, exhibit more improvement in lipid profile than yellow yam. Diosgenin control the hypercholesterolemia and improve lipid profile as it lowers low density lipoproteins and triglycerides. Diosgenin inhibits the cholesterol synthesis through the inhibition of HMG- CoA reductase (Shanthakumari *et al*., 2008; Imanningsih *et al*., 2014; Son *et al*., 2007). Therefore, both crude extracts of diosgenin from *D. alata* have been reported to enhance fecal cholesterol secretion and improvement in blood lipid profiles (Stewart *et al*., 2017; Harijono *et al*., 2016).

Conclusion

Dioscorea alata is the important plant with diverse bioactive compounds including steroidal sapogenin, flavonoids, polyphenols and tannins which are reported to be useful for the various disease conditions as anti-hyperlipidemics, anti-diabetics, anti-cancer, anti-apoptotic, anti-hypertensives, anti-inflammatory, anti-microbial, anti-fungal, anti-bacterial, anti-diarrheal, laxatives and cardio protectives. Therefore, it may act as a better alternative to synthetic drugs to treat various ailments.

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Conflicts of interest

None.

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