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APPLICATIONS OF *LAPORTEA INTERRUPTA* AS A TRADITIONAL THERAPEUTIC AGENT BY THE TRIBES OF TRIPURA AND IT'S POTENTIALITY IN PHARMACEUTICALS

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ABSTRACT: Tripura is a small hilly state in the northeastern region of India. The state has abundant precious plants with medicinal values, naturally increasing principally in hilly areas. The agro-climatic environment favors miscellaneous medicinal plants and is a hot spot for native medicinal plants. Many of the tribal peoples of the state are living in the deep forest area with adverse communication. From ancient times they have been using plant and their products to treat different body problems as they are familiar with the medicinal properties of locally available medicinal plants. Different parts of those medicinal plants are rich in different compounds and bioactive molecules like flavonoid, alkaloid, sterol, *etc*.. They use them in aqueous extract, raw, dried, or by preparing in different ways in patients suffering from different complications. The plant products protect against complications like indigestion, constipation, insomnia, chest pain, *etc*. *Laportea interrupta* is a plant that belongs to the Urticaceae family and is used by the tribals of Tripura as a therapeutic agent against several diseased conditions. The plant also has the potential to boost pharmaceutical products in the future.

INTRODUCTION: Among the two major groups of living organisms, plants are an important creature to regulate the function of the biosphere. Life would not be continued on Earth without plants. People depend on plants for basic human requirements, such as food, clothing, shelter, and medicine [1]. In this modern age, approximately 25% of the total drugs are prepared from plants and many others are artificial alternatives prepared on the model compounds purified from the plant species in current pharmacopeia [2, 3].

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According to the report of the World Health Organization (WHO), about 80% of the world population is concretely dependent on drugs based on plant substances [4], as a result, these practices is associated with the reduction of the side effects of self-medication [5].

World health organization documented that traditional medicine refers to health practices, moving towards knowledge and values incorporating plant, animal, and mineral-based medicine, religious therapies, physical techniques, and exercises, applied especially or combined to treat, detect and restrict illnesses or maintain well-being [6]. In developing countries, more than 80% of the population of the human need for initial health care is still conditioned on traditional medicines, most of which are plant-derived drugs.

Approximately 13% of 50,000 plant species used worldwide for medicinal purposes are angiosperms [7]. Among the 17,000 species of higher plants in India, 7500 species are well well-known for their medicinal uses in Ayurveda and are followed by 'Siddha and Unani', the oldest medical systems that have reported nearly 2000 species in the subcontinent of India. An age-old document named "The Charak Samhita", informed the construction of 340 herbal drugs and their native uses on herbal therapy [2, 3]. The Himalayan Region of India is well-known for its rich biodiversity. It supports about 18,440 plant species, where 8,000 species of angiosperms, 44 gymnosperms species, 600 species of pteridophytes, 1,737 no. of species of bryophytes, 1,159 species of lichens, and 6,900 no. of fungi species are present. 96.3% of Angiosperms, 3.0% of Pteridophytes, and 0.6% of Gymnosperms of this region are well-known for their medicinal values [7].

Northeast India is the highest reservoir of plant diversity in India and contains approximately 50% of India's entire plant diversity [8]. This part of India also contains 40% of India's endemic plant species [9]. This part of India has a massive diversity of life-saving medicinal plants and is a vital bio-resource. Several ethnobotanical studies were completed by different researchers [10, 11, 12, 13, 14] which is documented information on the distribution and the utilization of medicinal plants by native tribes. This is principally due to the residents of a variety of groups of trebles having their individual cultures and prosperous home-grown conventional knowledge. Tripura is a tinny hilly state located in the Northeastern region of India. It is bordered by Bangladesh on its three sides, excluding a small part in North-East India connected with Cachar district of Assam and Mizoram, with a prosperous diversity of flora and fauna different researchers [15].

Three distinct physiographic zones are there in the state, namely i) hill ranges ii) undulating plateau land and iii) low-lying alluvial land. More than 60% of the state is hilly, is roughly transverse by five major hill ranges in a north-south direction, and continues southward into Chittagong Hill Tract. The state's area is 10,497.69 sq km and is located between 22°7' and 24°2' North latitudes and 91°0' and 92°0' East longitudes with the Tropic of Cancer passing throughout it [16]. The state's climate is tropical as the Tropic of Cancer is passing across the state. The state's general weather is hot and humid with severe winter. The Agartala meteorological station records Tripura's average minimum and maximum temperature ranging between 16°C and 34°C, respectively [17]. The average annual rainfall in the state varies between 2, 250 mm and 2,500 mm. Depending on the palynological sequence, the study of Bhattacharyya *et al.,* 18 concluded that a significant alteration in the vegetation and area of human invasion vis-à-vis climate occurred over time. The vegetation of Tripura has not been constantly affected by climatic alterations as being situated close to the Bay of Bengal. With the initiation of agriculture in and around the state, the forests became more and more open with the extensive growth of herbs and shrubs [18].

With various types of languages, traditions and culture, 19 tribal groups have been settled down on different hilly regions of Tripura. Tripuri, Reang, Jamatia, Mog, Noatia, Chakma, Halam, Kuki, Lushai and Uchai are the main ethnic communities of the state [19]. Since the beginning, the tribal of Tripura were dependent on their adjacent forest not only for cultivation but also for various essential forest products for their existence. The food habit of the primitive ethnic communities of Tripura is dissimilar from the present. Lack of appropriate agricultural knowledge results in lower economic return. It bounds them on forest vegetables, wild fruits, tubers, leaves, roots, from their adjacent dense forest rich in flora and fauna. Rich natural resources like dense forests, plenty of medicinal plants and 19 ethnic groups thriving in harmony with nature can lure anyone to study the forest resources used by tribes in Tripura.

There are indeed many medicinal plants in Tripura whose potential activities have been established, such as anti-inflammatory activity, antioxidant capacity, cardiovascular boosting capacity, anti-microbial potentiality, anti-helmenthic activity, anti-cancerous activity, *etc*. We gathered the published literature on ethnobotanical plants from the Urticaceae plant family in Tripura, which ethnic peoples of Tripura use. Though all the 10 species of this family of Tripura have so many bioactive molecules and more or less medicinal impacts so, the aim of this review is to understand better the

current trends in research addressing the expansion of the agents from *Laportea interrupta* species, which is used against different diseases by the tribes of Tripura. The results of this review could facilitate to the provision of date knowledge about the therapeutic potentiality of *Laportea interrupta* plants and to develop existing knowledge lacking to develop future research by recognizing areas where more focus should be given.

MATERIALS AND METHODS: Electronically on various databases, most of the literature search was conducted, for example, SciFinder [20]. Supplementary information was gathered from reliable and genuine databases like PubMed 21, Scopus, Science Direct, Web of Science, the ecdysteroids and Google Scholar, and the electronic database (http://ecdybase.org). For this methodical review, the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guiding principle were followed [22]. Suitable and high-class publications were collected. Editorial letters, book chapters, abstracts of conferences, and unpublished results were not included. Only the articles written in English were included in this review preparation. Most important keywords used to prepare this review are phytoecdysteroids, phytoecdysones, ecdysteroids, ecdysones, secondary metabolites, phyto-insecticides, antioxidant, anti-inflammatory, anti-microbial, antidiabetic, anticancer properties, *in-vitro* and *in-vivo* studies.

Ethnobotanical Studies of Tripura: So far as the study of Tripura ethnobotany is concerned, very slight works is being conducted on this topic. However, some research articles are there associated with this topic are – an ethnobotanical survey on medicinal plants of Majumdar *et al.,* [23] documented 33 medicinal plants approved by tribal and non-tribal medicine men of Tripura state; in another study of Majumdar & Datta [24] documented 50 ethnomedicinal plants and their practice by Tripuri tribe in various disease conditions. About 170 ethnomedicinal plants of Tripura were used by different tribes of Tripura, and explaining the local spreading of mostly 184 medicinal tresses was acknowledged by Majumdar *et al.,* [25].

The ethnobotanical practices of plants by the Tripuri and Reang tribes of the state were reported by Das *et al.,* [26]. Das and Deb [27] documented 255 no. of plant species of Tripura which have medicinal values. The observation of Deb *et al.,* [28] explains the use of 39 medicinal plants by the Darlong community of Tripura. 86 plants with ethnomedicinal significance belong to diverse families reported in a study by Dey *et al.,* [29]. Pandey and Mavinkurve [30] have reported using 19 angiosperm and 1 Pteridophyte plant by the Chamka community of Tripura.

In a study by Shil *et al.,* [31] on native knowledge of medicinal plants practiced by the Reang tribes of Tripura to treat diseases reported a total of 125 medicinal plants species which belongs to 116 nos. of genera with 59 families were presented, which are used for the treatment of 42 different ailments. Majumdar & Gupta [32] reported 50 medicinal plants with their traditional uses of treatment among the tribes of Tripura. In a study of De [33] documented 25 nos. of plant species of Tripura with their application and medicinal impacts. Debbarma *et al.,* [34] documented 51 species of traditional medicinal plants of Tripura. In a survey by Shiddamallayya *et al.,* [35] in the forests of the North District of Tripura collected 223 plant specimens from 178 genera of 73 families and enlisted 98 medicinal plants with traditional practices.

Plant Species of Urticaceae Family and their Traditional Medicinal Uses in Tripura: The Urticaceae are a family of flowering plants comprising several renowned and valuable plants. According to the Royal Botanic Gardens database, this family has about 2,625 species grouped into 53 genera [36]. According to the Tripura Biodiversity Board, 20 species of 10 genera of this family plant are found in Tripura [37]. Among the 20 species of this family, those which are documented for their medicinal value in Tripura till today are described below below:

Laportea interrupta plant species of the family Urticaceae has medicinal value and is found in Tripura, reported by the study of Majumdar and Datta, [38]. The same study also reported that the root of the plant is used with leaves of *Eriocaulon cinereum* and *Holarrhena antidysentirica* in the ratio of 2:1:1 to prepare a formulation which has used for anti-inflammatory purposes by the tribes of Tripura [38].

Sarcochlamys pulcherima (Roxb.) is a shrub type of plant species belonging to the Urticaceae family. This plant has medicinal value and is found in the Dharamanagar and Kanchanapura sub-division forests of North District, Tripura [35].

Boehmeria macrophylla is a Urticaceae family plant used by the Reang tribes of Tripura and is locally known as Muithlimsu (in Reang). The decoction of its root is used to treat a female disease called leucorrhoea [31].

Oreocnide integrifolia (Gaud.) is a tree species of the Urticaceae family. It is found in Tripura and has medicinal uses by the tribal communities of the state [35].

Urtica dioica is a plant species of Urticaceae with a common name, Stinging nettle, in Tripura. The leaves of this plant contain bioactive molecules like flavonoids, tannin, volatile oil, etc., and are used by both the tribal and non-tribal communities of the state. According to the state's people, the leaf juice can treat the disease if used habitually after bath [29].

Boehmeria platyphylla is a wild type of plant species of the Urticaceae family, locally known as Uliatora in Bengali and Rojanti in Kokborok [24]. The documentation of Majumdar & Datta, [24] also explained that $^1/_2$ cup of its leaf infusion, along with slight sugar, is used to by the tribal communities of Tripura against acute dysentery.

Boehmeria macrophylla is a shrub plant species of the Urticaceae family with medicinal value found in the Dharamanagar and Kanchanapura sub division forests of North District, Tripura [35].

Urtica parviflora is a species which is commonly known as drona among the populations of Tripura. The plant is belonging to the Urticaceae family. It has medicinal property and its leaves are used to treat disease by the tribes of Tripura [27].

Debregeasia longifolia is a wild species of Urticaceae family of plants commonly found in Tripura and has medicinal properties. In a technical report, by Tripura Biodiversity Board, about the indigenous traditional knowledge of Tripura Majumdar & Gupta [32] reported that this plant is locally known as Thepanin Kokborok and Nicchia in Bengali, and its leaves are used by the tribes of Tripura. In this documentation, they were also reported that they administrated the tender leaves as vegetables during dysentery, and they apply crushed leaves paste as a poultice to treat arthritis [32].

Maoutia puya (Hook.) is a weed type of plant species belonging to the Urticaceae family. This plant has medicinal value and is found in the Dharamanagar and Kanchanapura sub-division forests of North District, Tripura [35].

Morphology and Distribution of *Laportea interrupta*: The plant *Laportea interrupta* is an annual herb up to 1 m. tall. It belongs to the Urticaceae family of the plant kingdom. The stems are a little woody at its base, frequently branched, with strewn stinging hairs up to 1.5mm. long, occasionally raised on protuberances ± 1mm. high; green to dark brown coloured bark. The habitat of the plant is lowland of rain-forests, mostly along with roads, riverine forests, as well as moist places in the wooded grasslands and is natively distributed in tropical regions of South Africa, the Arabian Peninsula, Mozambique, tropical & subtropical regions of Asia to NW. Pacific [39, 40]. The plant leaves have internally grooved petioles, broader on the way to the base, extremely close to the tip with a little groove, cuspidate just before the frontal part with a longer tip, and are also covered with hair-like structure and burning. In their small and divided peduncles flower grows [41].

Phytochemicals Constituents of *Laportea interrupta*: The extract of *Laportea interrupta* (whole plants) prepared in ethanol showed the occurrence of alkaloids, tannins, gums, reducing sugar, glycosides, flavonoids, and steroids [42]. The experiments of Selvam *et al.*, confirmed that phytochemical like saponin is found only in the aqueous solution of *L. interrupta*, but not in its methanolic extract, cardiac glycoside is found only in the methanolic extract of *L. interrupta*, but is not found in the aqueous extract of this plant, and the other phytochemicals which are available in both of the extracts of this plant are tannins, terpenoids, flavonoids and glycosides [43].

Traditional Medicinal uses of *Laportea interrupta*: *Laportea interrupta* is an ethnomedicinal plant that is found in the western

ghat region of India, including Tripura. The traditional healers and the tribes use different parts of the plant for the management of a variety of illnesses of humans [38, 44]. The people of Manokwari District, West Papua of Indonesia, use the leaves to treat malaria human body [45]. The root of the plant is boiled with water up to the boiling point, and by cooling, it is used twice a day for shower to treat dermatitis by the people of Kerela [44]. In the treatment of urinary diseases [46] and to treat the problem of impotency [47] this plant substances are used. Ethnomedicinally substances of this plant are used in West Africa to treat various problems like hay fever, chest problems, treating agent of blennorrhoea as a diuretics, headache, reduction in severe menstrual bleeding, arthritis treatment, management of anaemia, complications of kidney, as well as the pain management [48]. The Philippines traditionally use this plant to manage different problems such as cough, asthma, muscular pain and carbuncles [49]. It has been used conventionally in different countries to treat different female diseases like premenstrual complications, hormonal imbalance, osteoporosis, menorrhigia, *etc*. and male problems like prostate diseases [50].

Results of Different Experiments on *Laportea interrupta*: The result of this experiment of them [42] is tabulated below:

TABLE 1: DIFFERENT PHYTOCHEMICALS PRESENT IN *L. INTERRUPTA*

Name of the Phytochemicals present in *L. interrupta*		
Aqueous extract	**Ethanolic extract**	**Mthanolic extract**
Saponins, Alkaloids, Terpenoids, Flavanoids, Glycosides [43]	Alkaloids, Tannins, Steroids, Gums, Glycosides, Flavonoids, Reducing sugar [42, 51]	Alkaloids, Terpenoids, Cardiac glycosides, Flavanoids, Glycosides [43]

TABLE 2: DIFFERENT PHARMACOLOGICAL ACTIVITIES OF *L. INTERRUPTA*

Used materials of *L. interrupta*	Pharmacol-ogical activity	Study Substance	Positive Control	Effect	Mechanism	Ref.
Whole plant extract	Evaluated antioxidant activity	DPPH	Ascorbic acid	Antioxidant	Free radicalscaven-ging	[42, 52]
EE, PESF, CTSF & ASF extract of whole plant	Thrombolytic activity is evaluated	Human Blood	Streptoki nase	Thrombolysis	Lysis of blood clot	[42]
EE, PESF, CTSF & ASF extract of whole plant	Membrane stabilizing activity	Human erythrocyte	Acetyl salicylic acid	Survivability of cell	RBC haemolysis	[42]
EE, PESF, CTSF & ASF extract of whole plant	Evaluated cytotoxic activity	Brine shrimp	Vincristin Sulphate	Cytotoxicity	mortality rate of cells	[42]
Leaf decoction	Support of fetal-maternal health	female mice	Purified water	Support of fetal-maternal health	Increasing angiogenesis, fetal growth, and maternal health	[53]
Leaves	Treatment of malaria	Human	-	Cures malaria	-	[45]
Leaves	Relives pain	Human	-	Reduces muscular pain	-	[45]
EE, PESF, CTSF & ASF extract of whole plant	Evaluated anti-microbial activity	Various Gram +Ve and Gram -Ve bacteria	Ciproflox acin	Kills bacteria	Inhibition of bacterial growth	[42, 45]

EE = Ethanol extract, CTSF = Carbon tetrachloride soluble fraction, PESF = Pet Ether soluble fraction, ASF = Aqueous soluble fraction.

DISCUSSION: Antioxidants are artificial or natural substances with many health-beneficial potentials and may reduce or delay several types of damage to cells [54, 55]. They are found in various natural sources, including fruits and vegetables. They are associated with reducing and protecting against complications like cancers, coronary heart disease, diabetes, myocardial infarction, cardiovascular diseases, neurodegenerative diseases, osteoporosis, *etc.* [56, 57, 58, 59, 60]. Endogenous and physiological reactive oxygen species (ROS) are formed in the cell due to

oxidative stress, specifically as the by-products of oxidative chain reactions that occur in mitochondria [61, 62]. Generation of a reasonable quantity of ROS provides positive effects on maintaining homeostasis of the body, including the healing of wounds, pathogen killing, etc. But the excess formation of ROS disrupts the metabolic fucell's metabolic functions malfunctioning the concerned tissue, which leads to damage to the functioning organ's function Antioxidant substances can reduce and alter the changes which occur due to excess formation of ROS in tissues and prevent oxidative damage of the concerned organ [61, 63]. On the other hand, superoxide and hydroxyl radicals are the primary oxygen free radicals that are generated in various reduction reactions in the cell from molecular oxygen, and excess formation of them is also associated with the formation of plenty of diseases like cardiovascular complications [61], diabetes [65], stroke, cancer [66] *etc*. Different studies suggested that the effects of antioxidant substances alter all the changes associated with forming primary oxygen free radicals in the cell and protect different tissues from damage [61, 63]. Antioxidants are also reported to alter the changes in lipid profiles toward the normal range and prevent cardiovascular damage [61]. The studies of Uddin et al., 42 and Gruyal, 52 confirmed the presence of antioxidants in the Laportea interrupta extract by the free radical scavenging activity; it may reduce such types of metabolic damage in different tissues.

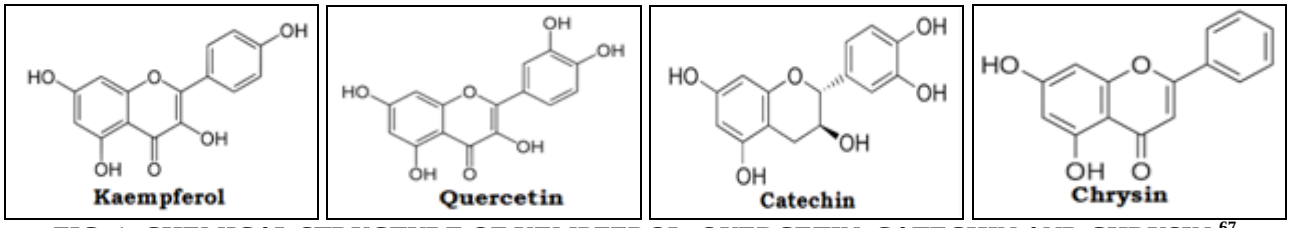

FIG. 1: CHEMICAL STRUCTURE OF KEMPFEROL, QUERCETIN, CATECHIN AND CHRYSIN [67]

The formation of blood clots inside the blood vessels, which prevents blood flow through the blood vessels, is called thrombosis. At the site of injury, platelets of circulating blood are gathered by playing a major role in developing thrombus, and coagulation of blood and are associated with the formation of thrombin and fibrin; leads to the damage of different organs and tissues due to the cessation of essential material supply to the target organ [68]. When it occurs in venous or arterial circulation, it creates major medical complications like myocardial infarction (heart attack) and strokes, the most common reason for death in the developed world [69]. In a study of Kiran et al, [70] on obstructive prosthetic valve thrombosis with streptokinase and tenecteplase statistically showed improved safety and earlier improvement by thrombolysis process. Plant materials that have antithrombotic properties are very much useful in the treatment of blood clots [71]. While the study of Jahan et al, [51] proved that the whole plant extract of *Laportea interrupta* has thrombolysis properties in human blood so, it may be used in the treatment of thrombosis. The cell membrane is an essential biological barrier for maintaining human homeostasis, and the breakdown of the stability of the membrane leads to the formation of different pathophysiological complications [72]. The body's internal environment is separated from the external environment due to biological barriers. It protects various disease formations like inflammatory bowel disease [73], coeliac disease [74] and graft versus host disease [75]. The results occurred due to the denaturation of membrane protein, inactivation of enzymes, etc., leading to changes in the permeability of the membrane and ultimately reducing ion flux, leaking of electrolytes, alteration in actual water content, construction of toxic components, and a common disturbance of homeostasis which inhibits cell survivability [76]. An important characteristic of multiple sclerosis pathophysiology is the blood–brain barrier breakdown. Dysregulation of blood the brain–brain barrier, mediated by the immune system, permits the passage of activated inflammatory cells into the brain; as a result, it induces demyelination, axonal failure, and damage of other tissues [77, 78]. The study of Jahan *et al.*, [51] by using human erythrocyte evaluated that the extract of *Laportea interrupta* prevents hemolysis of RBC and enhances the survivability of cells, so it can be used to maintain the normal homeostasis of cells and to prevent the

pathophysiology mentioned above. Cancer is one of the most shocking intimidations to mankind as it is the second leading cause of death worldwide after cardiovascular death. According to the study by Sung *et al.,* [79] new cancer cases are approximately 19.3 million, and about 10.0 million cancer-related deaths occurred in 2020 globally.

As the frequently diagnosed cancer subtype, breast cancer has overtaken lung cancer, through recent cases approximately at 2.3 million (11.7%), followed by lung cancer (11.4%), colorectal cancer (10.0%), prostate cancer (7.3%), along with stomach cancer (5.6%). Lung cancer still remained the chief reason of deaths related to cancer, with 1.8 million deaths approximately (18%), followed by colorectal cancer (9.4%), liver cancer (8.3%), stomach cancer (7.7%), and breast (6.9%) cancers of females [79]. The transfer of cancerous cells from one part to another part of the body is called metastasis. The expansion of metastases occurs due to the cancer cells departing their formation site, transport in the vascular system, continuous pressure in blood vessels, gathering at the new cellular environment of a secondary position, and getting away with a lethal struggle with the components of the body's immune cells [80, 81].

It is the hallmark of cancer responsible for the maximum number of deaths related to cancer [82]. Metastasis development is a highly multifaceted process that is a chief problem in cancer management. The cancer patients may extend metastasis after years or even a decade after the detection of the initial tumour develops, and the metastasis progression level becomes more complex [83]. Conventional anticancer chemotherapy is the process in which tumor cells are killed selectively by the use of cytotoxic drugs or by arresting the growth of cancerous cells permanently due to the interference of the drugs with the synthesis of DNA or by the damage of DNA by the chemicals of the drugs which ultimately lead to the death of the tumor cells [84]. Fewer efficiency and severe unpleasant effects are related with the conventional anti-cancer chemotherapeutics, and high drug resistance are the main drawbacks in the treatment and management of cancer [85]. All these complications are connected with the continuous conventional anti-cancer management such as radiotherapy, chemotherapy, and trans-arterial chemoembolization, necessitating alternatives, preferably natural products derived from plants.

Fascinatingly, plant anti-cancer natural products are not merely natural and comparatively safe. Still, they also exert multi-functional biological actions important for restoring several deregulated cell signaling pathways in different pathological conditions, including cancer. For illustration, various natural substances like as hispolon (derived from a therapeutic mushroom, Phellinus linteus) [86], oleandrin (derived from Nerium oleander) [87], catechins (derived from green tea) [88], apigenin, nobiletin, and tangeretin 89 have established multi-target anti-cancer property against large cancer phenotypic hallmarks together with invasion, cell proliferation, and metastasis [90]. Depending on these greater anti-cancer activities of natural products, predominantly from the plant kingdom have established a potential therapeutic agent against cancer [90, 91]. In their study, Jahan et al., 51, evaluated that the extract of *Laportea interrupta* has cytotoxic activity so it may have anti-cancerous properties.

Angiogenesis is the process that develops new blood vessels from existing blood vessels in the body [92]. Expect some pathological conditions; angiogenesis conducts wound healing to repair blood transport to the affected tissues after injury [93]. In the uterus of a female, it forms naturally at the time of the menstrual cycle or estrous cycle to convert the follicles that are ovulated into the corpus luteum to enhance the synthesis of progesterone hormone and to reconstruct the endometrium of uterus that receives the implanting embryos [94]. For this reason, angiogenesis needs endothelial passage, proliferation, and segregation of the pre-existing blood vessels inside because they support the capillaries to begin the construction of new tube-like structures and secondary dilatation of vessels to improve the circulation and uptake of nutrients [92]. Along with an increase in neighboring or systemic angiogenic factors with the breakdown of basement membrane and subsequently of endothelial tissue to provide convenience in the proliferation and endothelial migration, this multi-step process begins. With the engagement of smooth muscle cells, the differentiation of endothelium leads to the formation of tube-like structures which supports

mature vessels [95, 96]. The steps of angiogenesis that occur in the case of different organs, the same steps of this process such as proliferation, differentiation, and migration of endothelial cells, occur within the pre-existing micro-vessels of trophoblast [97]. Vasculogenesis is the process in which *de novo* vascular formation occurs during embryo formation. It starts with angioblasts (endothelial progenitor cells formation) in the allantois of the extraembryonic mesoderm of the female body [98]. Along with the expansion of placental morphogenesis, the vessel's formation in the placenta also expands throughout pregnancy [99]. In both the tissues of the maternal and fetal placenta angiogenesis occur in extensive mode. The placenta develops like an extensively vascularised 100 during the late gestation period of pregnancy.

Different studies on animals explored that, during the late gestation period, the enhanced blood flow through the placenta depends on angiogenesis and vasodilatation of the vessels of the uterus and placenta, which are very much vital for the usual growth, survival, well-being, *etc*. of the fetus, newborn baby and the pregnant mother [101]. In the placenta, widespread neovascularization is facilitated by the periodic increase in the inner part of uterus and the flow of blood during the gestation period. During the implantation and placentation of the fetus, the flow of blood occurs to the fetal, maternal, and placental units, during the connection of maternal-fetal circulations inside the placenta, progressively rises until the mid-gestation period of pregnancy, at that time considerably elevates at the final one-third segment of the gestation period, fundamentally maintaining the velocity according to the rate of the enlargement of the fetus [94].

As the study of Guzman *et al.,* [53] reveals that the leaf decoction of *Laportea interrupta* in female mice supports fetal-maternal health by increasing angiogenesis, fetal growth, and maternal health, so it may be a valuable substance for the above case. The vector-borne disease malaria is one of the most serious infective diseases in the world; it is troublesome for almost half of the population in the world and led to the death of hundreds of thousands of people [102]. Five species of single-celled eukaryotic protozoa, namely *Plasmodium* parasites, is responsible for the formation of this disease (mostly *Plasmodium vivax* and *Plasmodium falciparum*) and are transmitted due to the bite of female mosquitoes of *Anopheles spp*. [103]. After the entry of the malarial parasite into the human body, rupture of the first liver schizont of *plasmodium* and discharge of merozoites into the peripheral circulation shows the symptoms of the commencement of malaria infection in an ill patient and this phenomenon is silent for a huge number of patients who will be turned into sick clinically [104]. The presence of symptoms (fever) in the patients without clinical or laboratory signs to specify severity or the dysfunction of vital organs is defined as uncomplicated malaria [105].

During an early stage of malarial infection within the human host, ingestion of macrophage by merozoites, schizonts which are ruptured, or in the circulation the presence of antigen-presenting trophozoites or spleen leads to the liberation of TNF-α is occurs [106, 107]. Thus, the human clinical disease is the outcome of the interface of the preprogrammed biology of the parasite in concert with the pathophysiological feedback of human health [108]. Various fevers, anemia, and coma, among many others, are the final results of clinical [104, 109]. Among the different kinds of strategies to control malaria caused by the infections of *Plasmodium* in humans besides Long-lasting insecticide-treated bed nets (LLINs) and indoor residual insecticide spraying (IRS) relies on drugs [105]. Mass distribution of insecticide-treated bed nets among people provides grand success as a strategy to stop the spread of these parasites and has greatly reduced malarial deaths since the century turn [110]. Traditional health practitioners have used plants extremely to avoid or treat infections caused by *plasmodium* and near about 137 no. of plants belong to 48 families that they engage for this purpose [111].

As the study of Lense [45] evaluated that the leaf extract has anti-malarial properties, so it can be employed to prevent malaria.

A Major Medical Problem in the World is Muscular Pain: commonly 60% to 85% of the population has had back pain which has a non-specific muscular source for a few movements in lifetime prevalence) [112]. Chronic muscular pain is still a significant clinical problem which is understood poorly. Muscle pain occurs by the nerve

end plates, particularly for recognizing ischemia, mechanical forces, and tissue damage within muscle [113]. The pain is categorized as two types namely primary chronic pain if it is cannot be attributed to an identified disease or injure development directly, or as secondary chronic pain which is occurred due to a disease or process that straightly influence the bones, joints, muscles, and/or linked with soft tissues of the body [114]. The second type of group explains a collection of diverse states of pain occurred due to the infection, accumulation of crystal, and auto-inflammatory development which is responsible for continual local or systemic swelling and/or alterations of structures. Importantly it is also remarkable that the diseases of central nervous system is linked with harsh spasticity and can also result in musculoskeletal pain. These situations distribute a general thread of constant pain sustained daily, such as activity restriction and emotional suffering [115]. So, chronic pain of the musculoskeletal system has a major communal and emotional collision which comprises diminished socialization, incapability to work, failure of self-determination, nervousness, depression, and fear for the future [116]. A formation of excess amounts of reactive oxygen species leads to muscular fatigue and reduces the performance of the concerned muscles; supplementations of fruit-derived polyphenols are very useful to increase exercise performance by recovering the muscular damage [117]. As the leaf of *Laportea interrupta* prevents muscle pain, according to the report of Lense, [45], it can be used to manage such complications.

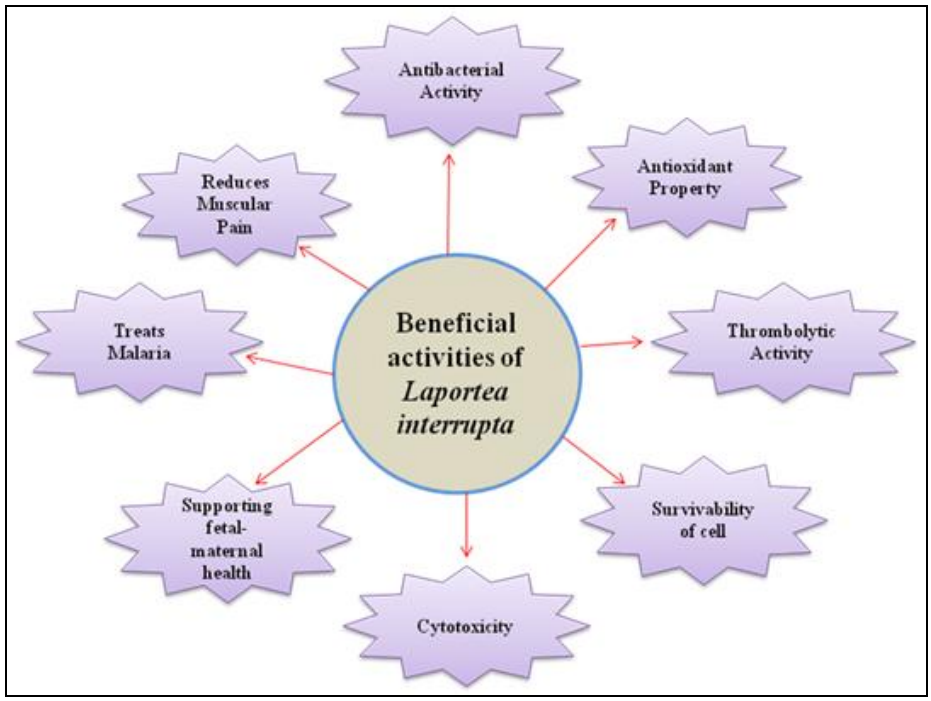

FIG. 2: BENEFCIAL ACTIVITIES OF *LAPORTEA INTERRUPTA*

Medicines prepared from plant substances have regularly been introduced to manage various diseases, including infections conducted by bacteria and fungi [118, 119]. Progressively, various anti-microbial mechanisms are developed by plants to defend them from communicable diseases, generally by manufacturing compounds with anti-biofilm and bacteriostatic activities without biocidal consequences [120]. The compounds with anti-microbial properties from plants with medicinal value may reduce the growth of the organisms like bacteria, fungi, viruses, and protozoa by diverse mechanisms in respect to those of which are currently used as anti-microbials and possibly with an important clinical significance in the management of microbial strains which are resistant [121]. Some anti-microbial substances can inhibit protein synthesis by altering bacterial ribosome subunits and are very effective in combatting infections conducted by bacteria [122]. DNA gyrase is an enzyme vital for bacterial DNA's synthesis, replication, repair, and transcription processes. Therefore, some anti-microbial compounds provide anti-microbial

activity by altering the activity of the gyrase enzyme [123]. Transglucosilases and trans-peptidases are the enzymes that are mainly associated with the formation of cell wall of bacteria. Some of the anti-microbial agents bind with the peptide substrate of the peptidoglycan layer of bacterial cells as a result it prevents enzyme reaction and leads to the disruption of cell wall formation of bacteria [124].

For many research groups, searching for new phytochemicals from kingdom plantae, with anti-microbial properties is the vital goal oriented with chemistry and pharmacology of medicine [125]. Studies of Uddin *et al*, [42] and Lense [45] showed that the extract of *Laportea interrupta* has anti-microbial activity, so it can be used to identify the phytochemicals which has anti-microbial activity and present in it.

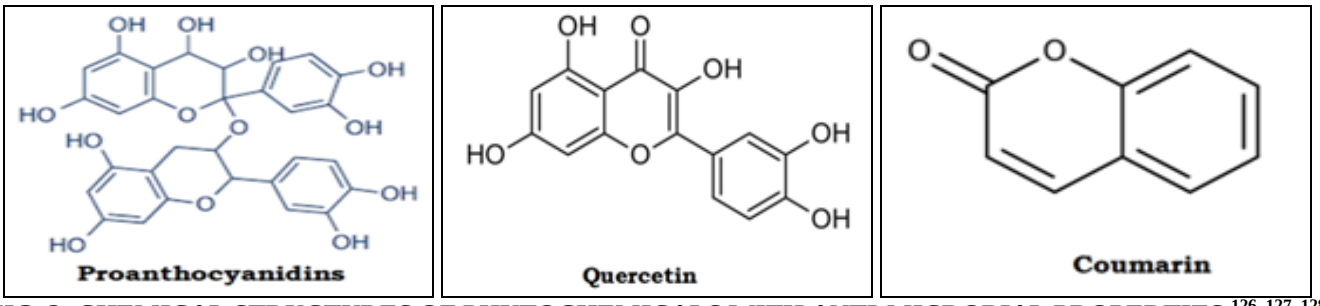

FIG. 3: CHEMICAL STRUCTURES OF PHYTOCHEMICALS WITH ANTI-MICROBIAL PROPERTIES [126, 127, 128]

CONCLUSION: Different properties of *Laportea interrupta* plant, is explained in this review, reported from 1981 to 2021. The diverse bioactive properties of *Laportea interrupta* plants like antioxidant, antimalarial, thrombolytic, cytotoxic, membrane stabilizing, anti microbial activity *etc*. **Fig. 2** are reported here. Besides these, various mechanisms by which various plant substances perform their medicinal actions is also discussed.

However, although abundant research was conducted on this plant over the past three decades, most of the outcomes mentioned in this current review are based on the survey types of works with very limited *in-vivo* and clinical studies. This review explains the potentiality of biological and medicinal properties of the different parts of the plant, which may be utilized in the pharmacological development at the end of various confirmatory researches on their efficacy and safety.

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