Original Article

PLANT LATEX: PHYTOCHEMISTRY, MEDICINAL PROPERTIES AND APPLICATION – A REVIEW

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Abstract

Latex, a milky fluid contains proteins, alkaloids and other metabolites, normally exuded at the time of injury. The color of the latex differs from plants to plants where the color are white, yellow, orange etc. These latexes have enormous application in medicine and industries. In this review, various of sources of latexes and its chemical composition are described. Its role in defence and their applications in the field of medicine, nanotechnology is highlighted.

Keywords: Latex; chemical composition; bioactivity.

Introduction

Latex is the biological fluid produced naturally by the elongated secretory cells in a diverse range of natural plants as secondary metabolites, called laticifers. Laticifers which are the longest plant cells are found only in latex-bearing plants due to their elongation growth. They assemble into tubing structures containing latex, making up the laticiferous system[1]. They are distributed in various parts of plants mainly bark, stems, roots, fruits, and leaves of up to 20000 flowering plants (angiosperms) species from more than 40 families. The production and storage of latex within the laticifers generate the turgor pressure. Whenever the plant is damaged, the latex leaks aplenty in response to the turgor pressure within the laticifers[2]. The physical characteristics of latex are divided majorly into colour, stickiness, exudation, and clotting effects. Different plant species yield different colours of plant latex (Table 1). Their colour is mainly non-transparent milky white. Some plant lattices can be transparent or in certain colours such as orange, yellow, and scarlet. Their colours are not representing any of their specific biological functions but they may be changed when exposed to the air[2]. The different plants which exude latex are list in Table 2.

Table 1: Different colours of Plant Latex

Color of Latex	Plant species with latex	References
Milky White	Rubber tree (*Hevea brasiliensis*, Euphorbiaceae)	[4]
	Papita (*Carica papaya*, Caricaceae)	[5]
	Poppy (*Papaver somniferum*, Papaveraceae)	[4]
	Fig tree (*Ficus carica*, Moraceae)	[4]
	Milkweed (*Asclepias syriaca*, Apocynaceae)	[4]
Pale Yellow	Wild fig trees (*Ficus septica*, Moraceae)	[4]
Milky Yellow	Celandine (*Chelidonium majus*, Papaveraceae)	[6]
Orange	Wild fig trees (*Ficus benguetensis*, Moraceae)	[4]
Scarlet	Dragons blood (*Croton lecheri*, Euphorbiaceae)	[7]

Table 2: The common name, scientific name, and family of different latex bearing plants.

Common name	Scientific name	Family
Anjeer	*Ficus carica*	Moraceae
Autograph tree	*Clusia glandifolia*	Cluciaceae
Avelós	*Synadenium umbellatum*	Euphorbiaceae
Badi Dudhi	*Euphorbia hirta*	Euphorbiaceae
Ban tulsi	*Croton bonplandianum*	Euphorbiaceae
Bargad	*Ficus bengalensis*	Moraceae
Biodiesel plant	*Jatropha curcas*	Euphorbiaceae
Bush Allamanda	*Allamanda schottii*	Apocynaceae
Chalate	*Ficus insipida*	Moraceae
Common fig	*Carica cardamarcensis*	Caricaceae
Coralbush	*Jatropha multifolia*	Euphorbiaceae
Dragons blood	*Croton lecheri*	Euphorbiaceae
Gazyummaria	*Ficus macrocarpa*	Moraceae
Gular	*Ficus glomerata*	Moraceae
Hierba mala	*Euphorbia cotimfolia*	Euphorbiaceae
Hyaena-poison	*Hyaenanche globosa*	Euphorbiaceae
Mexican Poppy	*Argemone ochroleuca*	Papaveraceae
Milk weeds	*Asclepias sp.*	Asclepiadaceae

Night Jasemine	*Allamanda blanchetti*	Apocynaceae
Oleander	*Nerium oleander*	Apocynaceae
Opium poppy	*Papaver somniferum*	Euphorbiaceae
Papita	*Carica papaya*	Caricaceae
Pili kaner	*Thivetia nerrifolia*	Euphorbiaceae
Rose Periwinkle	*Madagascar periwinkle*	Apocynaceae
Rubber tree	*Hevea brasiliensis*	Euphorbiaceae
Salaad patta	*Lactuca sativa*	Asteraceae
Sandhill milkweed	*Asclepias humistrata*	Asclepiadaceae
Sapthaparna	*Alstonia macrophylla*	Apocynaceae
Sapthaparna	*Alstonia scholaris*	Apocynaceae
Spurge	*Euphorbia characias*	Euphorbiaceae
Sucuba	*Himatanthus articulates*	Apocynaceae
Sudha	*Euphorbia nerrifolia*	Euphorbiaceae
Tridhara	*Euphorbia antiqunum*	Euphorbiaceae
White frangipani	*Plumeria rubra*	Apocynaceae
Wild fig	*Ficus virgatalatex*	Moraceae

The stickiness of distinct plant latex protects them after having minor injuries from attack of herbivorous insects. Its viscosity not only destroys the mouth part but the whole body of the insects. The plant species which have the sticky latex are lettuce, *Lactuca sativa,* and rubber tree, *Hevea brasiliensi* while the non-sticky latex-bearing plant species are oleander tree, *N. indicum,* and mulberry tree, *Morus spp*. The more viscous the plant latex, the stronger its defence functions. Plant latex becomes more viscous after its exudation and eventually gets clotted[4]. The amount of the latex exudation depends on the parts of plants. Theoretically, the young leaves and raw fruits of the plants exude more latex than the mature leaves and ripe fruits. For instance, an unripe papaya fruit exudes more latex compared to other parts of the papaya trees like stem, leaves, and ripe fruits[5]. Also, different types of species from the same genus and family can have different amounts of exudation. Bauer *et al*.[8] stated that the exudation of *Asclepias barjoniifolia* latex from the young leaves is four times more than the exudation of *Asclepias angustifolia*. Likewise, the exudation of *Ficus benguetensis* is non-transparent orange which is very small in amount, whereas its other species such as *F. virgata* and *F. variegate* produce non-transparent white latex in larger amount[8]. *Calotropis gigantea* secretes white coloured latex (Figure 1).

Figure 1. Latex secreting *Calotrpis gigantea*

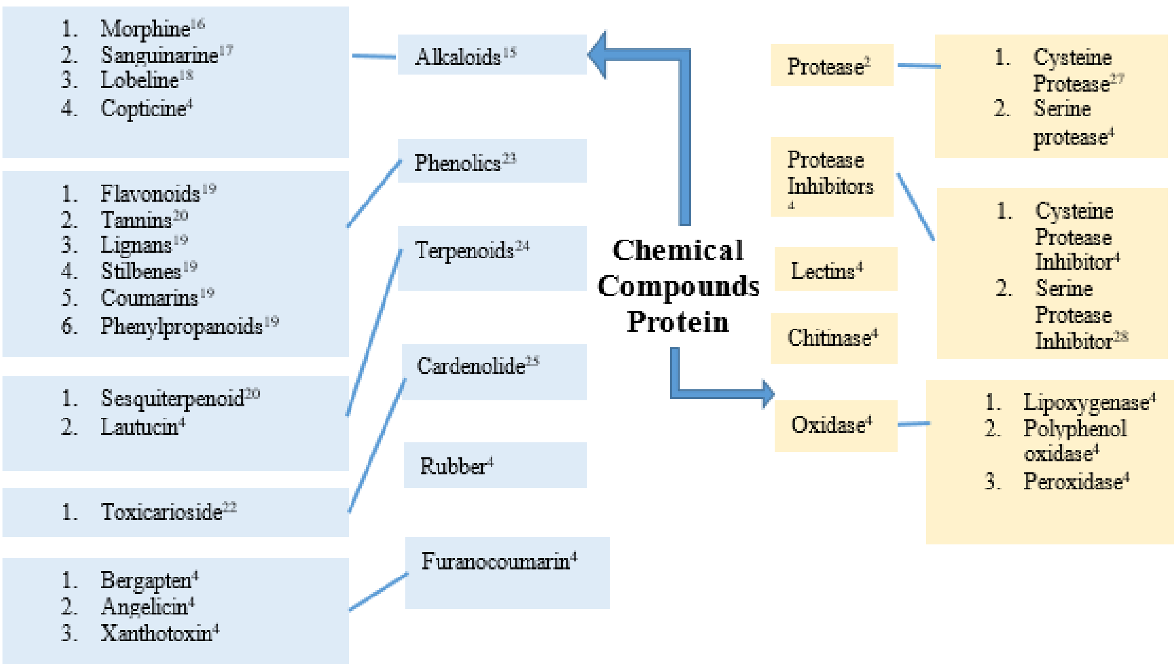
Basically, the plant latex contains numerous chemical and protein compositions to play some important roles. Latex as a complex emulsion comprises basic components like sugars, proteins, fats, organic acids, essential oils, sterols, and mucilage (gum). The chemical compositions include alkaloids, phenolics, terpenoids, cardenolides, rubber, and furanocoumarins while proteomic compositions include several proteins and enzymes[9]. They undoubtedly serve as defence mechanisms and plant internal interaction. However, they also have different functions in the fields of industry and medical sciences. They are widely used for production of raw materials in our daily life such as gloves, catheters, condoms, car tyres, pacifiers, and balloons and many other diagnostic materials. To date, these bioactive chemicals in plant latex with various biological activities such as antimicrobial, anti-carcinogenic, anti-oxidants, anti-inflammatory, anti-proliferative, vasodilatory, and insecticidal activities are gradually involved in pharmaceuticals and pesticides products for therapeutics purposes[10].

Chemicals and proteins compositions of plant latex

Generally, plant latex is made up of carbon, hydrogen, and nitrogen with a molecular formula of C_3H_3N. Those compositions may differ between the plant species classifying into chemical and proteomic compositions. The phytochemicals are produced through primary and mostly secondary metabolism. They are also called the complex mixture of secondary metabolites of plants. Basically, there are sugars, fats, organic acids, essential oils, sterols, mucilage, rubber, and resins[11]. Additionally, the chemical compounds include alkaloids, terpenoids, cardenolides, phenolics, rubber, furanocoumarins, acetogenins, and saponins (Figure 2). The enzymatic proteins included are papain, proteases, lipases, oxidases, peptidases, chitinases, glucosidases, plasmin, thrombin, hevein, peroxidases, and phosphatase[12].

To date, the roles of those chemicals and proteins are still in ongoing research but their main role are absolutely to provide defences against the invasion of bacteria, viruses, fungi, protozoa, nematodes, and herbivores insects through various biological activities[13].

Figure 2. Chemicals and proteins found in various species of latex-producing plants



Alkaloids

Alkaloids are the alkaline compounds with low-molecular weight and nitrogen-containing within a heterocyclic ring structure[14]. They are one of the secondary metabolites mostly found in latex of diverse higher plants. The well-known plant alkaloids are morphine, sanguinarine, lobeline, nicotine, quinine and so forth. The concentration of the alkaloid contents depends on the parts of the plants, climate, and geographical areas[15]. Alkaloids are found in some families of latex-producing plants such as Euphorbiaceae, Papaveraceae, Moraceae, Apocynaceae, and Campanulaceae in high content. The first discovered alkaloid is morphine from the opium poppy, *Papaver somniferum* of Papaveraceae family in 1804[15]. Morphine is the main content of the latex in opium poppy [16] where reported to be as 5 % of fresh weight or 25 % of dry weight as well as poppy seeds[29]. Other opium alkaloids include thebanine, papaverine, codeine, and noscapine [29]. Morphine are reported to bind and activate the μ-opioid receptor (MOR) and acts as the phenanthrene opioid receptor agonist in human CNS. Morphine chiefly exerts analgesic and sedative values towards CNS or gastrointestinal tract of vertebrates. However, when MOR is activated, there will be associated symptoms like euphoria, respiratory depression, and physical dependence[30-31].

Sanguinarine, another well-known alkaloid, is also found in several plant latex. For example, Croaker *et al.*[17] stated that the thick red latex of bloodroot *Sanguinaria canadensis* from their rhizomes contains mostly sanguinarine as well as other alkaloids like sanguilutine, chelerythrine, protopine, and allocryptopine. These protect the plants as sanguinarine is toxic to vertebrates or insects, as it can disrupt neurotransmission, DNA synthesis, and choline acetyltransferase[32].Sanguinarine is the well-known inhibitor for activation of NF-κB3, a nuclear transcription factor which regulates cell growth, cell cycle, and apoptosis. Facchini *et al.*[33] stated that sanguinarine are found abundantly in the roots of opium poppy, *Papaver somniferum* which serves as the deterrent against the pathogens or herbivores insects. Thus, they were reported with properties of antifungal, antimicrobial, anti-inflammatory antiviral and cytotoxic activities [33-34].

Lobeline is also a piperidine alkaloid found in the latex and leaves of genus *Lobelia* especially cardinal flower, *Lobelia cardinalis* from Campanulaceae family [18]. It is in powder form which is white, amorphous, and soluble in water in its pure form. lobeline's target is nicotinic acetylcholine receptors (nAChR) which influence the reuptake of serotonin and dopamine by acting as either agonist or antagonist of nAChR[35]. Typically, intake of lobeline by vertebrate can induce several symptoms such as coughing, nausea, vomiting, diarrhea, weakness, mental confusion, increased blood pressure, tremors, and seizures. Tamargo *et al.* [36] also reported that the therapeutic index of lobeline is narrow indicating that its potentially beneficial dose is close to its toxic dose.

Commonly, alkaloids along with other secondary metabolites in plant latex help in accelerating the rate of plant reproduction. They also serve as the defence strategies against biotic and abiotic stress including releasing the toxic targeting neurotransmission and damage repairing through antioxidant activity[37]. In order to protect the plant from herbivores, they possess characteristics such as bitter flavour, protein disruption mechanism upon ingestion or metabolization, and central nervous system (CNS) disruption[38]. The natural plant alkaloids from latex also attract the flower visitors through its stimulant properties. This function is crucial to enhance the survival chance of the plants. Simultaneously, this type of plant alkaloid allows several biological activities for human therapeutics purposes including antioxidant, antitumoral, anti-inflammation, and stimulants[39].

Phenolics

Phenolic compounds are one of the main classes of secondary metabolites produced by several plant species. They are distributed into polyphenols and phenolic acids. The structure of phenolic compounds consists of an aromatic ring with benzene and one or more hydroxyl groups[23]. Examples of phenolic compounds are flavonoids, tannins, lignans, stilbenes, lignin, coumarins, phenylpropanoids, and anthraquinones. There might be organic solvent soluble, water soluble, or completely insoluble[19]. According to Tungmunnithum *et al.*[23], there are over 8000 of plant phenolic and flavonoids occupy half of them, which is the largest group among the phenolic compounds. They are synthesized through different pathways such as shikimic acid, methylerythritol phosphate, malonic acid, and mevalonic acid pathways. Among them, shikimic acid pathway is the most important pathway for phenolic compounds production [40]. Flavonoids are the common phenolic compounds with low molecular weight making up with 15 carbon atoms configured in C6-C3-C6. There are 2 aromatic C6 rings and heterocyclic rings including an oxygen atom. Accurately, flavonoids are synthesized by polypropanoid from phenylalanine molecules. Flavonoids are divided into 6 subgroups namely flavonones, flavonols, flavanones, flavan-3-ols, and isoflavones[41]. Tannins, in contrast, are the phenolic compounds with relatively high molecular weight making up with a chemical structure of 2 to 3 phenolic hydroxyl groups on a phenyl ring [20]. Their sizes are quite large. They are subdivided into hydrolyzable and condensed tannins. There are other tannins like coffee tannins, phlorotannins, and labiatae tannins[42].

Phenolic compounds are present in plant latex in huge amounts. For instance, Ismun *et al.*[43] reported that there are naphthoic acid, gallic acid, chlorogenic acid, quercetin, and rutin found in the latex of rubber tree, *Hevea brasiliensis*. These components are included in the total phenolic contents[43]. Moreover, the latex of sweet potato, *Ipomoea batatas* from Convolvulaceae family are known to have high concentration of the phenolic components like eicosyl esters of p-coumaric acids, octadecyl, and hexadecy. The latex from the roots of the sweet potato is 10%, which is higher than the other parts like vine with 3%[44]. Likewise, observation of Snook *et al.*, (1994) revealed that weevils are more susceptible towards high concentration of Z-isomers of C16, C18, and C20 coumarates in the latex. This defense role is apparent against different herbivore insects[45]. Rampadarath *et al.*[46] claimed that the latex of *Jatropha curcas* from Euphorbiaceae family consists of different phytochemicals including flavonoids and tannins which contributes in antimicrobial and larvicidal activities. Lin *et al.* [47] stated that different phenolic compounds in plants play their respective roles. Primarily, they serve as antioxidant or anti-radical scavenging systems. Free radicals are generated from the metabolic processes, environmental pollution, or ultraviolet radiation. As in Abdul-Hafeez *et al.*[48] phenolic compounds in the plant serve as reducing agents, hydrogen donors, radical scavengers or singlet oxygen quencher to protect the plant cells from those oxidative damages. They also act as attractants to attract the pollinators for reproduction or repellent to deter the harmful pests[49]. For example, the study of Ghasemzadeh and Ghasemzadeh,[50] stated that flavonoids are one of the chemicals which give the plant attractive taste so that the fruit dispensers are attracted to spread their seeds for reproduction.

Moreover, phenolic compounds like flavonoids serve as the ultraviolet screen or filters which reduce the damage of UV radiation from penetrating the plants[51]. Flavonoids like anthocyanins are reported in Younis *et al.*[52] to protect the plant cells from DNA damage induced by solar radiation. They are also able to exert free-radical scavenging activity like the antioxidant activity to avoid accumulation of these harmful compounds. Of course, they minimize the excitation pressure which is potentially oxidation susceptible. As other chemical compounds in plant latex, phenolic compounds also act mainly as a defence chemical by providing mechanical support for the latex-producing plants and preventing excessive water loss from the plant body. For instance, tannins and phytoalexins as the defence chemical compounds which allow plants to control invading microorganisms[53]. Furthermore, phenolic compounds like lignin also act as structural polymers found in latex of vascular plants which is one of the major components of plant cell wall[54].

Terpenoids

Terpenoids or isoprenoids including rubber (*cis*-1,4-polyisoprene) are the abundant naturally occurring organic chemicals found in different parts of plant including latex. This class of compounds are derived from the isoprene with 5 carbon and isoprene polymers, terpenes. The class of terpenoids consists of several isoprene structural units classifying into monoterpene, sesquiterpene, diterpene, triterpene, tetraterpene, and poly-terpene[24]. They are synthesized from two major pathways called 1-deoxy-D-xylulose-5-phosphate (DXP) pathway and MVA pathway. Both pathways produce a main metabolite intermediate called isopentenyl diphosphate. Of these, DXP pathway synthesizes the monoterpenes, diterpenes, and tetraterpenes which occurs primarily in plastids. MVA pathways in contrast, occur in cytoplasm and synthesize secondary metabolites including sterols, sesquiterpenes, and triterpenes [55]. Terpenoids are found in many plant species which are up to 300 genera and 8 families. Currently, over 50000 terpenoids have been discovered[56].

Sesquiterpenoids are one of the terpenoids found in latex-producing plants. Primarily, they serve as the defence mechanism. Firstly, they are antifeedant in which the lactucopicrin and 8-deoxylactucin in sesquiterpene lactones can deter the feeding of herbivores insects or birds, especially locusts. Sesquiterpenes also serve as antimicrobial agents to prevent growing of microorganisms. For example, inhibition of growth of *Cladosporium herbarum* that is pathogenic and able to cause plant diseases[21]. Additionally, Chadwick *et al*.[57]also stated that latex of the cultivated lettuce called *Lactuca sativa*, Asteraceae consists of sesquiterpenoids or specifically sesquiterpene lactones including lactucin. They are present abundantly in laticifers or rarely in vacuoles of other plant cell types.

Another well-known terpenoids, lactucin also found in plant latex to induce the trenching behaviour in caterpillar *Trichoplusia ni* from Noctuidae which cut a narrow trench across leaves[58]. The phorbol, a plant-derived organic compound from the family of diterpenes and its derivatives are present in the latex Euphorbia species such as *Euphorbia biglandulosa, Euphorbia tortilis* and *Euphorbia neriifolia* [59]. Along with diterpenoids, they are considered toxic to insects and other animal consumers which they can promote tumour and induce dermal inflammation[60]. Meanwhile, they also exert several effects namely allelopathy, a phenomenon in which an organism produces biochemicals for growth, development and reproduction of other organisms, and stimulation of germination in their parasitic plant like Orobanche[57].

Cardenolides

Cardenolides are a type of steroid found in plant latex, which are also termed as cardiac glycoside or cardenolide glycoside. They possess sugar, lactone moieties, and steroids. They are constructed by 5- or 6- membered lactone rings at C17 in β position[25]. Typically, cardenolides are often toxic with heart arresting properties. The toxicities are capable of inhibiting the activity of Na^+ or K^+ ATPases which are involved in the regulation of ion concentration and maintenance of electric potential in cells of animals or insects. Specifically, they influence neurotransmission. The mechanism of action is mainly due to the binding of cardenolides to the Na^+ or K^+ ATPases through their membrane extruding part. Nevertheless, several species of insects which feed on the cardenolide-producing plants have developed the cardenolide-tolerance Na^+ or K^+ ATPases. This is because these species are having single amino acid substitutions in their cardenolide-binding sites[61].

The one and only role of the cardenolide component in plant latex is to be a defence mechanism against the herbivorous insects and pests. For example, Züst *et al*. [62] stated that the latex of plants from Apocynaceae such as milkweed plants (*Asclepias* spp.) consists of cardenolides as one of their defensive tools. Cardenolides are concentrated in their latex but also present moderately in leaves. However, the concentration of cardenolides depends on the plant species. For instance, *A. californica* possess a small amount of cardenolides in latex but concentrated in leaves. Moreover, Dai *et al*.[22] revealed that there were new nor-cardenolides called toxicarioside isolating from the latex of Moraceae species, *Antiaris toxicaria* from tropical areas of Southeast Asia. It has been used as the dart or arrow poisons as depicted in Carter *et al*.[63]

Proteases

There are numerous proteins and enzymes present in plant latex. In recent literatures, proteases, chitinases, oxidases etc are reported. Their existence in plant latex are to provide signal transduction, oxidative defence and external defence against natural enemies[4]. Of these, protease, peptidases, or proteinases is the richest and commonest proteins found in plant latex. Different families of latex-producing plant species are reported to possess at least one proteolytic enzyme. In the early 1900s, over hundred types of plant latex proteases are isolated and characterized to discover their proteolytic activities. They are known to hydrolyse various peptide bonds of protein-substrates such as collagen, fibrin, fibrinogen, gelatin, casein, and so forth. Proteases are divided into endo-peptidase and exo-peptidase. Endopeptidases carry out of hydrolysis activity at the non-terminal amino acids within the protein while exopeptidases carry out the hydrolysis at the carboxyl ends or amino[26].

Most of the proteases found in plant latex are classified as cysteine and serine proteases. For example, cysteine proteases are found in latex of *Caricaceae*, *Apocynaceae*, and *Moraceae* while serine proteases are found in *Euphorbiaceae*, *Convolvulaceae, Apocynaceae,* and *Moraceae*. Aspartate and metalloprotease are found rarely in certain species of plant latex. There are no threonine, asparagine, and glutamic proteases discovered so far in plant latex[4].

Commonly, latex of papaya tree, *C. papaya* is known to consist of 69-89% of cysteine protease among the total protein. A famous cysteine protease enzyme of papaya is called papain [27]. Other cysteine proteases include ficin and bromelain. Somavarapu *et al*.[64] reported that the plant cysteine protease found in latex of *Vallaris solanacea* shows proteolytic activity which can be inhibited by *p*-chloromercuribenzoate. Sobottka *et al*.[28] revealed that the proteases isolated from Euphorbiaceae family such as *Euphorbia selloi*, *Sapium glandulosum*, and *Euphorbia papillosa* are classified as serine-protease class. Their proteolytic activities are significantly inhibited by serine protease inhibitors. Similarly, Mauritanicain, a protease isolated from latex of *Euphorbia mauritanica* shows high proteolytic activity towards casein substrates[65]. Moreover, cotinfolin, a metallo-protease which is rare in nature, can be isolated from the latex of Caribbean copper plants called *Euphorbia cotinifolia*. They are claimed to possess some essential metal atoms for the catalytic activity. It is a high molecular mass molecule which can be inhibited by metallo-specific inhibitors namely o-phenanthroline, EGTA (ethylene glycol-bis(β-aminoethyl ether)-N,N,N′,N′-tetraacetic acid) and EDTA (ethylenediaminetetraacetic acid)[66]. In addition, Raskovic *et al*.[67] stated that latex of fig such as *Ficus carica, Ficus religiosa, Ficus bengalensis* are rich in collagenolytic proteases as well as chitinolytic enzymes. Of these, except for the common cysteine proteases, an unusual aspartate-protease are also isolated from latex of *Ficus religiosa* as mentioned in study of Devaraj *et al*.[68] .

To date, the exact roles of the proteases in plant latex are still not well-understood. Researchers found that they are likely to be the defence mechanism against herbivore insects and pests especially in papaya tree, *C. papaya* and fig tree, *F. carica*. The toxic mechanism usually targets the midgut or body cavity of the insects after consuming the part of the latex containing proteases. For instance, Konno *et al*. [69] stated that cysteine protease in papaya latex protects the plant against the lepidopteran larvae, especially the *Samia ricini* from Saturniidae. After feeding the latex with cysteine proteases, the young instar of *S. ricini* dies and its dead bodies will become soft and black after 6 hours. The suggested that the consumed proteases exert their toxicity or hydrolysis at their potential targets which are the insect tissues that contain proteins.

Applications of Plant Latex

With different components found in plant latex, they are widely applied to satisfy the need and want of mankind. Over the years, uses of plant latex have been discovered in the field of industry, medicine, and nanotechnology. Since ancient times, plant latex has been a great application in production of basic necessities of humans. For example, natural rubber, the main and largest components obtained from plant latex, is used to manufacture different products needed in our daily life. These are processed in the rubber industry[70]. In addition, plant latex is also applied for medicinal uses. Traditionally, the tribal communities apply plant latex as pharmacological purposes for burns, wound healing, joint pain, treatment for worm infections or other skin diseases[71].Medically, the dried latex of some plant species can be used as analgesic and non-analgesic alkaloids such as morphine, codeine, papaverine, and noscapine. Sometimes, it is also linked in production of illegal drugs like heroin[72]. The derivative latex called styrene is also widely used in the field of immunoassay to prepare the immunodiagnostic materials such as ELISA plates[73]. The mixture of components in plant latex also exert numerous biological activities especially antibacterial, antifungal, anti-parasites, anticancer, antioxidant, and anti-inflammatory[10]. Application of nanotechnology most fields is gradually prevalent in which the plant latex is able to associate with nanoparticles to enhance their antimicrobial activities[74].

Rubber Industry

Rubber, alternatively called terpenoid is an abundant chemical component found in the latex-producing plants which occupies up to 40% of latex[75]. Natural rubber latex is a biopolymer with a molecular formula of $(C_5H_8)n$ and a chemical structure of *cis*-1,4-polyisoprene. Its molecular weight is 100000-1000000 daltons. However, the head and end groups structure is still unclear. They are milky white and sticky. The stickiness of latex helps to protect latex-producing plants from herbivore insects that attack them at any parts by gluing the whole insects or mouth parts. Also, its sticky exudation prevents the infection of related pathogens [76]. Generally, the components found in the natural rubber latex include rubber, polyisoprene, proteins, sterol glycosides, fatty acid, resin, ash, water, and sugar [75]. As in the study of Abraham and Ramesh,[77] the size of rubber particles ranged from 0.02 to 3.0mm. Their shape is mainly spherical and rarely pear-shaped or oval and they are negative charged. There are also phospholipids and a layer of adsorbed protein to protect the rubber suspension which ensure the colloidal stability to plant latex. Notably, approximately 0.05% of trace metals are also found associated with rubber particles such as copper, potassium, and magnesium. Its density is around 975-985kgm^{-3} and pH of 6.5-7.0[77].

The use of rubber was first discovered in Mesoamerica due to their indigenous cultures in the 16th century BC. Olmec, the major civilization of Mesoamerica used the rubber extracted from *Hevea brasiliensis* and made balls for their cultural ballgame[78]. Then, applications of rubber were started introducing all around the world such as insulating objects like wires and waterproof objects like vehicle tires and footwears. These encourage the rubber manufacturing industry[79].

There are 300 genera of plants from 8 families containing the rubber component in their latex over the years. To date, *H. brasiliensis* is still the major source for the rubber industry. It is also termed as Brazilian rubber tree or para rubber tree as it originated from the Amazon river basin[80]. The preference of this species is due to their easy-to-grow characteristics as this species is well-growing when cultivated in a number of tropical countries such as Malaysia, Thailand, and Indonesia. Also, the rubber contents exist in the fresh latex of rubber trees in high concentrations which meet the needs of mankind[81]. This natural rubber is used in more than 40000 products in the earth due to its excellent properties like water resistance, tensile, electrical insulation, heat resistance, tear resistance, good abrasion, and resilience[82]. The well-known products that are made from natural rubber latex are vehicle tires, surgical gloves, mattresses, rubber band, footwears, chewing gums, to name but a few[77]. Possessing the outstanding characteristics of tear resistance, electrical insulation, and good abrasion, study of Braihi *et al*.[83] reported that natural rubber is effectively used for protecting metal surfaces of petrochemical storage tanks against the corrosive and erosive media. This was done by coating a thin layer of rubber film upon the surface of metallic parts such as tires, O-rings, conveyor belts, body parts, spare parts, body sealing systems, and fluid transfer system. Furthermore, blending of two or more rubbers was claimed to provide apparent protection from harsher conditions like high acid, brine, and temperature. In a recent study, Naphon *et al*. [84] proved that the properties of natural rubber can be up-levelled when employed with nanoparticles. For example, mixtures of nanoparticles, TiO_2 into the natural rubber enhances the thermal conductivity and meanwhile reduces the electrical resistivity of the electrical wire insulator and thus decreases the hot spots that cause melt and fire.

Apart from Hevea rubber tree, there are guayule, Russian dandelion, fig tree, and rubber rabbitbrush known to be rubber-producing plants. However, only guayule and Russian dandelion yield large amounts of natural rubber in their latex. These species are considered the alternative rubber sources for the rubber industry whenever there is shortage of Para rubber tree, especially during the World War II [80]. Guayule, *Parthenium argentatum* from the family of Asteraceae is the shrub found commonly in the north plateau area of Mexico. As a plant species originating from Chihuahuan Desert, it can grow in harsh environments[85]. Guayule usually grows with temperature ranging from 18-50°C and low rainfall areas such as desert[86]. Stonebloom and Scheller,[87] reported that *Parthenium argentatum* is easier to be cultivated against broad temperature and climates compared to *Hevea brasiliensis.* Its production of natural rubber has higher molecular weight than the Hevea rubber. Rasutis *et al*. [86] reported that Guayule rubber is a good alternative source for natural rubber which they are currently made into medical and personal hygiene products such as gloves, condoms, cosmetics, and wetsuits thanks to its hypoallergenic properties. Guayule rubber is also suitable to be the raw materials for vehicle tires due to its high molecular weight[86, 88]. In fact, it is an important source contributing in the rubber industry but it contains more impurities compared to Hevea rubber tree making it a not too good rubber source[86].

Russian dandelion, *Taraxacum koksaghyz* is another good option for rubber. It was discovered in 1931 in Kazakhstan. Russian dandelion produces latex which exhibits the same quality of natural rubber as rubber trees. However, their latex content is low. Russian dandelions contain rubber in their flowers, leaves, and roots, which root is the best extraction part for high quantity quality[89]. There is high demand for natural rubber as raw materials nowadays from the major source of the natural rubber, Hevea rubber tree. Dandelion has the potential to become an excellent alternative which shares the same applications as Hevea rubber tree but reduces the dependence of rubber from Asia. This is a significant advantage for the rubber industry as this source is economic and less carbon emission[90]. Cornish, [91] reported that the chemical and physical properties of Russian dandelion rubber allows manufacture of good-quality and resilient tires as those made from Hevea rubber and definitely better than Guayule rubber. However, russian dandelion rubbers are not suitable for medical application and only suitable in conventional use like tires or dry rubber applications as it can elicit hypersensitivity [90] just like Hevea rubber tree. This is because the rubber particles in the latex of Russian dandelion contain more associated proteins which can trigger the allergic reaction especially in Type I latex sensitized patients[92].

Medicine

Latex plays an essential role in medical fields. The most basic latex products are medical gloves which are life saviours for medical staff as well as scientists. Latex gloves are commonly used because they are high durability and sensitive during touching. Latex gloves are manufactured from latex collected from natural rubber trees. Natural latex itself is a chemical characteristic of high resistance to acids, bases and formaldehyde. Hence, medical gloves provide a good barrier production. This allows healthcare workers, especially doctors and nurses as well as patients to be protected from infection. Utilization of medical gloves can reduce the risk of contamination of blood borne pathogens and environmental contaminants. Dentists wear gloves during examining the oral cavity of their patients to protect themselves from bacteria in mouth [93]. Latex gloves also protect the patient since there is a case in the 1990s, a Californian girl developed AIDS after oral examination by her dentist with HIV without wearing gloves. AIDS can be transmitted through body fluids and gloves able to provide a barrier for both patient and dentist [94]. Gloves are suggested to be worn whenever contact with patients especially when handled with blood, body fluids, mucous membrane as well as broken skin[95]. For laboratory personnel, latex gloves reduce the permeation of chemical substances which are corrosive [96]. However, latex gloves may cause skin hypersensitivity for those with natural rubber latex allergies. They developed skin reaction of localized pruritus, irritant contact dermatitis and generalized urticaria. Natural latex gloves can be replaced with hypoallergenic gloves to reduce hypersensitivity[97]. Catheterization is a method to reduce urinary retention in patients with urological surgery. Transurethral catheterization is urinary catheter inserted into urethra while suprapubic catheterization is catheter inserted into an artificial track created between bladder and abdominal wall[98]. Foley indwelling catheter is the main equipment for catheterization. It is typically made up of latex or silicone [99]. Latex catheter is the first catheter manufactured from natural rubber which was invented in the 1930s[100]. Latex catheter with the characteristic of highly waterproof, flexible and excellent in resilience so it is widely used. However, it may lead to urethral strictures since latex is cytotoxicity. Latex catheter is also more susceptible to urinary tract infection and biofilm formation. *E. coli*, *Klebsiella pneumonia* and *pseudomonas aeruginosa* are common urinary tract infection bacteria. These conditions can be evaded by using latex catheters which are coated with polymer such as silicone and biocidal coating such as silver coating[101].

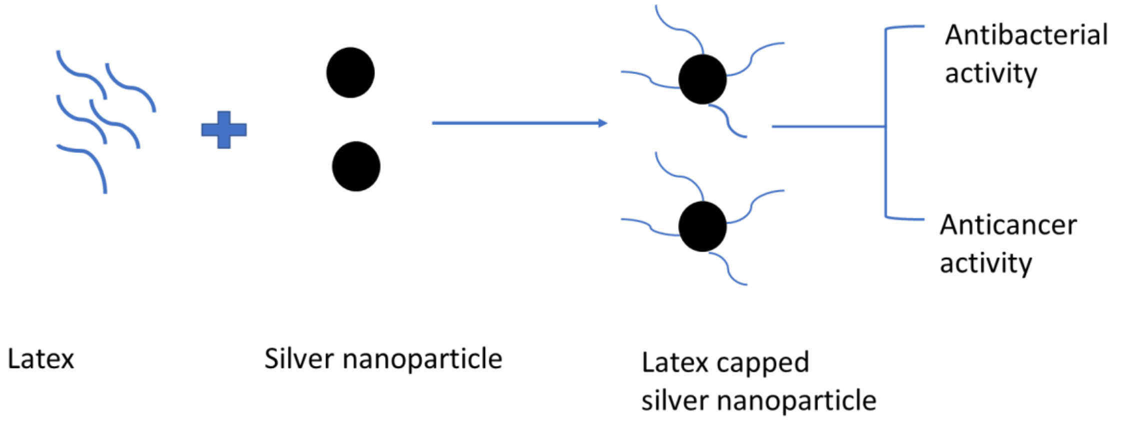
Tourniquet is a compressive device which manages the venous and arterial circulation. There are two types of tourniquet which are non-inflatable tourniquet and inflatable tourniquet. Non-inflatable tourniquets are made up of latex. Traditionally, a tourniquet is used as limb saving devices for the military. It was tight at the limb during injuries to occlude blood flow thus preventing blood loss and limb trauma. Tourniquet is also widely used in orthopaedic and plastic surgeries. It creates a bloodless surgical area and reduces perioperative blood loss by blocking the blood flow. Susceptibility of the surgery also can be improved since the surgeries are safe and accurate [102]. However, usage of non-inflatable tourniquet may lead to latex anaphylaxis in patients with latex allergy [103].Since there are modern tourniquets, currently non inflatable tourniquets are lesser to be used [102].

Nanotechnology

In nanotechnology fields, latex is largely utilized especially for nanoparticles synthesis. Recently, green synthesis of nanoparticles is promptly encouraged since it is more eco-friendly and less contact with chemical substances. Rupiasih *et al*.[104] successfully synthesized silver nanoparticles from latex extract of *Thevetia peruviana*. Latex acts as a reducing and capping agent in the synthesis of silver nanoparticles from silver nitrate ($AgNO_3$). Apart from that, latex itself normally have specific characteristics which improve the effect of nanoparticles. Latex of *Thevetia peruviana* consist of thevetin which are used as heart stimulants. However, direct consumption would cause poisoning.

Chandrasekaran *et al.*[105] had been studying fabricating silver nanoparticles with *Carica papaya* latex (Figure 3), where it was possessing antibacterial and anticancer activity. Similar to Rupiasih *et al.* [104] they also added double distilled water to latex but they centrifuged the mixture and used the supernatant instead of the mixture of latex and distilled water. Silver nanoparticles synthesized with *C. papaya* latex possessed antibacterial activity for both gram positive and gram-negative bacteria.

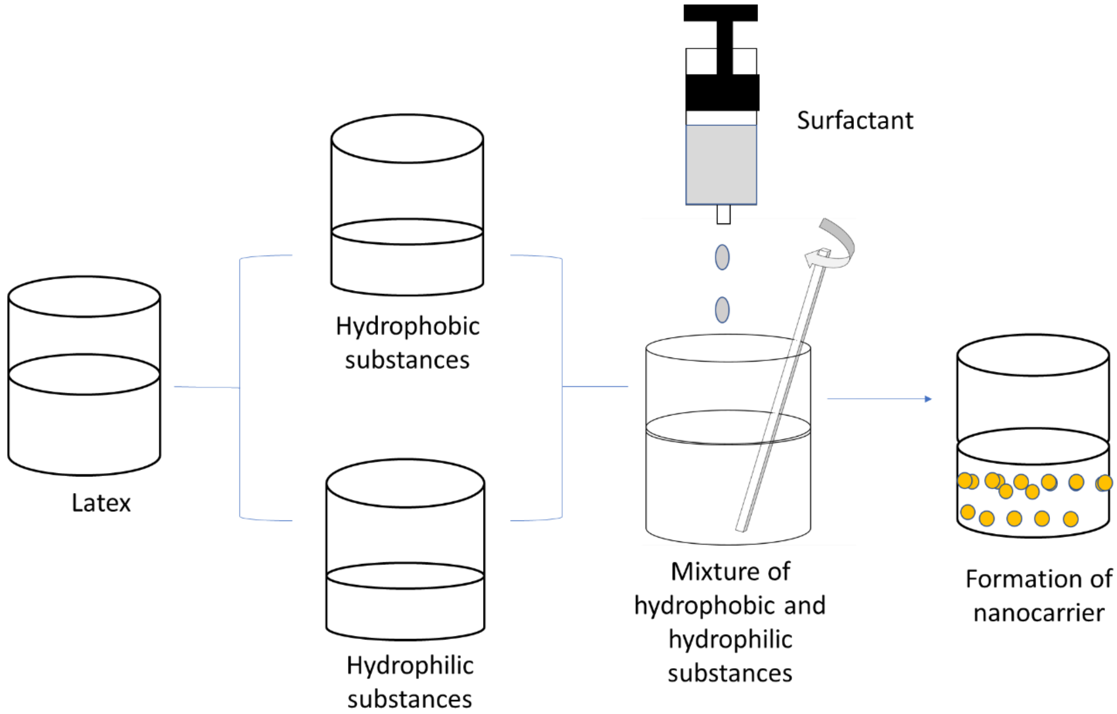
Figure 3. Reduction and Functionalization of CPAgNPs by *Carica papaya* latex [105]



Additionally, there are research studies on drug delivery with inorganic nanoparticles that are more efficient. 5-Fluorouracil (5-FU), a chemotherapy drug for lung cancer acts greater effect when loaded to papain-inspired gold nanoparticles. Hence it renders gold nanoparticles possessing anticancer activity. Gold nanoparticles and 5-FU act synergistically to maximize the efficacy of drugs. Since nanoparticles with novel physiochemical properties and nanoscale in size, they are able to gain maximum success in the drug delivery system compared to the drug itself[106].

Latex of *Calotropis gigantea* L has been used to synthesis silver nanoparticle with antibacterial and cytotoxic effects [107]. Furthermore, latex-based hybrid nanocarriers were synthesized from *C. gigantea* where the polar and nonpolar compounds dissolved in methanol and petroleum ether respectively then the mixture was added with either any of following surfactant such as cetyltrimethylammonium bromide (CTAB), Sorbitanmonolaurate (Span-20) and Tween 20 as explained in Figure 4. Doxorubicin loaded nanocarriers were formed by loading the drug to the hybrid nanocarrier[108]. Drug loaded nanocarriers demonstrated higher drug effects than doxorubicin itself [108]. Likewise, Samrot et al. [109] produced curcumin loaded nanocarrier using latex of *Calotropis gigantea* and *Euphorbia antiquorum.*

Figure 4. Production of hybrid nanocarriers using latex



Bioactivity

Antibacterial activity

Natural latex rubber from *H. brasiliensis* exhibited inhibitory activity against Gram positive *Staphylococcus aureus* and Gram-negative *E. coli* [110]. Hevein, a protein extracted from latex of *H. brasiliensis* which is rich with cysteine. It is responsible for antimicrobial activity especially *candida spp.*[111]. Its antibacterial activity can be enhanced by adding chitin[112]. *H. brasilensis* even demonstrated antifungal activity against *Cryptococcus neoformans* and *Trichosporon cutaneum*. Furthermore, latex of *Argemone ochroleuca* (*A. ochroleuca*) possessed antibacterial activity against *Bacillus subtilis, Enterobacter aerogenes, Micrococcus luteus, E. coli* and *Staphylococcus aureus*. It also exhibits antifungal activity against candida species and range of phytopathogenic fungi. Its antibacterial activity is contributed by the presence of isoquinoline alkaloids in *A. ochroleuca* such as sanguinarine and berberine[113]. Mechanism of its antibacterial activity is by disturbing the FtsZ protein in the filament to be assembled. FtsZ protein normally is functioning to form the contraction belts. Bacterial fission is then restricted, membrane permeability increased and bacterial DNA are even intercalated. Sensibility of *S.aureus* towards ß-lactamic antibiotics can be increased by sanguinarine [114].

Traditionally, *Jatropha curcas* latex are used for wound healing since it promotes angiogenesis activity[115]. *J.curcas* consists of saponins and tannins which effectively inhibit growth of common human pathogenic bacteria such as *Salmonella typhi, Klebsiella pneumoniae, Morganella morganii, E. coli* and *Listeria monocytogenes* [116]. *J.curcas* also show remarkable inhibitory activity against *Streptococcus mutans* due to secondary metabolites such as flavonoids[117]. Jatropha latex significantly inhibit the growth of multidrug resistant bacteria such as *methicillin-resistant Staphylococcus aureus* (MRSA) and carbapenem-resistant *Pseudomonas aeruginosa* (CRPA)[118].Calotropain, mudarin and calactin are components in latex of *Calotropis procera* which are responsible for bactericidal activity[119]. They show inh3ibitory effects to *E. coli, Staphylococcus aureus, Staphylococcus albus* and *Streptococcus pneumonia*[120]. *Calotropis procera* latex even contains terpenoids, cardiac glycoside, tannins and phenolic compounds[121]. Alkaloids, steroids, cardiac glycosides and terpenes also can be isolated from *Calotropis gigantea*. These phytochemical substances are responsible for antibacterial effects against few cariogenic bacteria such as *Streptococcus mutans* and *Lactobacillus acidophilus*[122].

Traditional treatment for skin infection is using latex from *Ficus carica* since it is composed of hexanic and hexane ethyl acetate extracts. These components are able to inhibit replication of viruses, especially herpes simplex type 1 (HSV-1), echovirus type 11 (ECV-11) and adenovirus (ADV)[10]. Coumarin is one of the bioactive components from latex of Tunisian caprifig which are responsible for antimicrobial activity. Antibacterial activity of fig latex is due to the free hydroxyl group at position 7 while the antifungal activity is contributed by 6-OH in coumarins. Coumarins may prevent human immunodeficiency virus (HIV) since it inhibits DNA gyrase which is related to activity inhibit HIV[123]. Fig latex also can be used as intracanal medicament against *Enterococcus Faecalis* which infect dentinal tubules[124]. This is due to fig latex highly containing polyphenols, benzaldehyde and flavonoids. *Ficus sycomorus* contains tannins, saponins, reducing sugars, alkaloids and flavanones aglycones. These bioactive constituents play the role in antibacterial activity[125]. Proteins and proteolytic enzymes which are commonly isolated from plant latex capable of lysing the cell wall of bacteria and acts bactericidal effects [126].

Latex of *Aloe Harlana* Reynolds acts as antimicrobial agents against Gram negative such as *E. coli*, *Vibrio cholera* and *Salmonella typhi*. Aloin and 7-O-methylaloeresin A in its latex are responsible for its antibacterial activity[127]. Aloin A have been formulated into ointment with polyethylene glycol for skin disease and wound healing since it possessed strong inhibitory effects against bacteria[128]. Antimicrobial activity of *A. harlana* is enhanced due to the presence of functional groups on phenyl rings of anthraquinones. Carboxyl, hydroxyl and hydroxyl methyl are functional groups present. Mode of action of this latex is by targeting the surface-exposed adhesions, cell wall polypeptides and membrane bound enzymes. Thus, bacterial cell membrane permeability increased and intracellular contents leaks. Consequently, apoptosis occurred[129].

Anticancer activity

Latex is a traditional method for cancer treatment. Variety of latex having different anticancer properties. Latex from fig exhibited anticancer properties. A cysteine proteinase, ficin can be extracted from the latex of *F. carica*. Ficin is an enzyme which does not have cytotoxicity to normal cells but causes cancer cells to apoptosis. Other proteinase which act similarly with ficin are caseinolytic and gelatinolytic enzymes. There is other anticancer agent presence in latex of fig which is palmitoyle derivative of 6-*O*-acyl-β-D-glucosyl-β-sitosterol[130]. Protocatechuic acid which is isolated from fig latex also restricts the metastasis of cancer cells as well as reduce invasiveness of cancer cell lines as well as induce apoptosis[131]. Latex of fig consists of phenolic compounds such as polyphenols and flavonoids so it also possesses antioxidant activity. This latex can inhibit angiogenesis which is good for cancer formation. Anti-angiogenesis effects are indicated by decreased tumour necrosis factor alpha, prostaglandin E2 and vascular endothelial growth factor[132]. According to Hashemi *et al.*[133] Latex of *F. carica* inhibits the proliferation of stomach cancer cell lines. *F. carica* latex can be used in cervical cancer treatment. There are studies demonstrating that latex from *F. carica is able* to inhibit the growth of cervical cancer cells and suppress clonogenic ability of cervical cancer. In cervical cancer, Ki67 protein is a cell proliferation marker. Hence, cell proliferation of cervical cancer cells can be inhibited by targeting Ki67 protein. Cell progression of cancer cells are then restricted. Latex from fig induces apoptosis at Sub G1 and thus arrest cell cycle [134]. Fig latex even reduces the survival rate of HeLa cells.

Natural rubber latex from *H. brasiliensis* not only possessed antibacterial properties, it even exhibited anticancer activity. C-serum which is anti-proliferation can be extracted from the natural rubber latex. C-serum greatly affecting human breast cancer cell lines (MDA-MB-231), human liver adenocarcinoma cell (HepG2) and human ovarian carcinoma (A2780)[135]. Latex significantly arrests the cell cycle and triggers apoptosis. Apoptosis is indicated by prolonged cell cycle at G0/G. Damaged DNA is replicated and thus prevents the cell entering the S phase[136].

Madagascar periwinkle is a medicinal plant which traditionally used for treatment of cancer, liver infection and rheumatism. It is even used as calming drug. It contains variety of alkaloids. The major dimeric alkaloids in *Catharantus roseus* are vinblastine and vincristine[137]. These two alkaloids possessed anti-cancer properties by inhibiting angiogenesis which enhance growth of tumour. Vinflunine, derivatives of vincristine and vinblastine acts as microtubule-targeting agents. They bind to tubulin and thus interfering the formation of spindle from microtubules by polymerization[138].These actions resulting in anaphase onset inhibited. Consequently, the cell cycles are arrested in senescence-like G1 phase or prolonged state which then rapid apoptosis occurred[139]. Hence, they act as anticancer drugs and administered into patient via intravenous. These two alkaloids exert significant anticancer effects to a variety of cancers, especially multi-drug resistant cancer. Vincristine are specially used for leukemia treatment in pediatric while vinblastine as treatment for Hodgkin's disease. It also can be used for human neoplasma, skin cancer and breast cancer[140].

C. procera which exhibited inhibitory activity to bacteria also demonstrated anticancer properties. Cardiac glycosides can be extracted from latex of *C. procera*. It specifically targets the human lung, cervical cancer cell line and even MGF-7 breast cancer cell. The mechanism of cardiac glycosides on MGF-7 cells is cardiac glycosides capable of interfering plasma membrane Na+/ K+- ATPase as well as act as antagonists to oestrogen receptors. Apart from that, reactive oxygen species (ROS) are generated due to the presence of cardiac glycosides. Cardiac glycosides act on cancer cells by decreasing their glycolysis. Thus, the production of NADPH which can remove ROS in cancer cells is also reduced. Permeability transition pore of mitochondria opening largely affected by low concentration of ROS. Once it's induced, higher concentrations of ROS are released. Increased intracellular ROS concentration resulting in intracellular calcium ions concentration increased, DNA damaged and MCF-7 cell apoptosis induced. Furthermore, autophagy in cancer cells are also triggered by ROS. Cardiac glycosides such as bufalin, digoxin and ouabain are very effective in anticancer activity[141].

Croton celtidifolius is an antitumor plant used in Brazil for a long time. It contains red latex which is typically used for treatment of oral ulcers, diabetes as well as cancer. Latex of *C. celtidifolius* rich with flavonoids and phenolic compounds such as myricetion, quercetin and kaempferol. Quercetin activates apoptosis by inhibiting HSP70 protein which related to cancer cells survival. Cell death consequently is induced in K562, Molt-4, Raji and MCAS cells. Kaempferol induced Bax and Bad, pro-apoptotic molecules to promote antiproliferation of A549 cells. Latex of *C. celtidifolius* also contain lignin which exhibit antiproliferative activities. It acts synergic with flavonoids which possess anti-tumour effects. Lignins arrest G2/M cell cycle through p53 pathways. Flavanols and flavan-3-ols act on DNA by intercalating between the base pair and thus resulting in DNA cleavage. These significantly inhibit the activity of cancer cells[142].

Anti-inflammatory and Analgesic activity

C. procera is a medicinal plant with multiple functions. Its latex is a potent anti-inflammatory agent. Latex fraction of it contains osmotin and peptidases effectively treating oral mucositis [143]. Anti-inflammatory activity of its dry latex exerts by restricting the liberation of mediators which increased vascular permeability such as histamine, prostaglandins E2, bradykinin, serotonin and 5-HT. Thus, vascular permeability decreased and fluid exudation were prevented [144]. Latex of *C. procera* effective in preventing both cellular infiltration and carrageenan-induced oedema. Subsequently, inflammation is inhibited[145].

Traditionally, latex of *Hancornia Speciosa* are used for treating warts, acne and inflammation. Similar to *C. procera, H. speciose* exert inhibitory effects on mediators released. Formation of oedema are divided into two phases. Phase 1 releases of bradykinin, serotonins and histamine while phase 2 is released of prostaglandins.

Movements of these mediators are restricted to reach the sites of injured and thus their pharmacological effects are inhibited. *H. speciose* also exhibits strong anti-oedematogenic effect on paw oedema due to receptors for mediators being directly blocked. Since there are no significant effects on phase 1, latex of *H. speciose* directly blocked inflammatory receptors instead of nociceptive receptors. Serum protein vascular leakages are inhibited since *H. speciose* latex minimizing both the volume of exudate and concentration of exudate proteins. Latex of *H. speciose* also inhibits PGE2 pathway and thus possesses anti-inflammatory activity. It also inhibited the migrations of inflammatory cells which secreted cytokines and nitric oxide[146]. Expression of nitric oxide synthase and cyclooxygenase 2 also elevated by the latex[147].

Latex of *Himatanthus sucuuba* containing triterpenes which exhibited anti-inflammatory and analgesic activity. These triterpenes are lupeol acetate, alpha-amyrin and lupeol cinnamates[148]. Latex from *Himatanthus drasticus* showed both anti-nociceptive and anti-inflammatory activity[149]. Janaguba milk is the latex collected from *H. drasticus*. It's similar to *H. sucuuba*. Janaguba milk containing a lupeol pentacyclic triterpenes which can be synthesized into bioactive components such as lupeol acetate, beta-amyrin and beta- sitosterols. Lupeol acetate in latex responsible for pain relief at both neurogenic pain and inflammatory phases through opioid system. Opioid antagonist naloxone are totally blocked by lupeol acetate. Lupeol acetate also demonstrates antiedematogenic activity induced by carrageenan[150]. Lupeol acetate also significantly inhibits myeloperoxidase released by activated human neutrophils. Inhibitory effects on migration of neutrophils decreased the response from nociceptive which stimulated by stimuli. Nitric oxide synthesis in plasma commonly associated with infiltration of neutrophils. Subsequently, the number of iNOS cells also reduced. This indicated that pro-inflammatory cytokines and nitric oxide system are involved in anti-inflammatory activity.

Ficus bengalensis also known as Banyan tree. Latex of *F. bengalensis* are tonic, reduced inflammation and aphrodisiac. Traditionally, its latex is used to treat anemia, gastrointestinal disorders, liver disorder, dysentery, nose disease and gonorrhea[151]. Therefore, it can also be used as an anti-inflammatory and analgesics agent. Its extracts contain tannins, terpenoids and flavonoids. Flavonoids molecules inhibit enzymatic activity of phospholipase A2, cyclooxygenase and lipoxygenase. Consequently, production of inflammatory chemicals which are involved in the late phase of pain perception such as leukotrienes, prostaglandins and arachidonic acids are significantly decreased. Other enzymes such as protein kinase C, protein tyrosine kinases and phosphodiesterase are also restricted. Phospholipase A2 is also inhibited by terpenoids and this resulting prostaglandin synthesis is suppressed[152]. Anti-inflammatory effects of *F. bengalensis* are similar to non-steroidal drugs for analgesics such as phenylbutazone. *F. carica* also can be used to treat inflammatory disease[153]. *F. carica* inhibits both production of nitric oxide and tumour necrosis factor alpha (TNF- α) to exert anti-inflammation[154]. Its anti-inflammatory activity may be enhanced due to presence of flavonoids and steroids[155]. Flavonoids and phenolic compounds are antioxidant compounds which decrease the induction of oxidative stress and inflammation. These resulting in refrained white blood cells from increased[132].

Lactuca virosa is also known as wild lettuce. It is classically used as a sedative, analgesic and antispasmodic agent. It is preferred in comparison to opium since it does not interfere with the function of the liver and digestive system. Its demonstrated sedative and analgesics effect are due to it containing sesquiterpene lactones which are lactucopicrin and lactucin[156]. Lactucin and lactucopicrin bind to GABAA receptors and result in sleepiness [157].

Antioxidant activity

As mentioned before, latex of *curcas* containing phenolic compounds and polyphenolic compounds with antioxidants activity. Polyphenolic compounds included proanthocyanidin, flavanols and flavonoids exhibit strong antioxidant activity. Major phenolic compounds are flavan-3-ols with antioxidant and anticancer properties. Its anticancer properties enhanced by antioxidants activities. These antioxidants subsequently promote wound healing[158]. *F. carica* latex also similar to *J. curcas* is a natural antioxidant. Apart from that, *Euphorbia tirucalli* typically are used in cancer treatment. Its latex contains polyphenols included anthocyanin, resveratrol, tannins, epigallocatechin-3-gallate, gallic acid and proanthocyanins[159]. Hence, it has stronger scavenging activity on free radicals than *F. carica* and *F. sycomorus*[160]. *Euphorbia hirta* also similar to *E. tirucalli* can act as antioxidant agents.

Latex of *C. papaya* is also a well-known antioxidant. Triacylglycerol lipase is isolated from latex *c. papaya*[161].*Cryptostegia grandiflora* also possessed antioxidant activity and this property associated with its anti-inflammatory activity[162]. Latex of *Pedilanthus tithymaloides* demonstrated antioxidative activity attributed to its kaempferol 3-O-beta-D-glucopyranoside-6"-(3-hydroxy-3-methylglutarate), quercitrin, isoquercitrin, and scopoletin[163]. Orange latex of *Chelidonium majus* are good antioxidants since it is rich with chelidonine, chelerythrine and sanguinarine[164]. *F. bengalensis* also demonstrated antioxidative and free radical scavenging activity[165].

Anti-protozoan activity

Latex of *Euphorbia resinifera* and *Euphorbia officinarum* demonstrated antileishmanial and antitrypanosomal activity. This is because *E. resinifera* contains alpha-euphol and alpha-euphorbol and *E. officinarum* contains obtusifoliol and 31-norlanosterol. Mode of actions against *Leishmania* are inhibiting synthesis of proteins or nucleic acids. Membrane-associated calcium-dependent ATPase pump[166]. Latex collected from the leaf of Aloe calidophila Reynolds also showed the activity against Leishmania. Aloinoside, aloin and mircodontin are anthrones extracted from Aloe calidophila Reynolds and these anthrones possess strong antileishmanial activity[117].

Latex of *Aloe macrocarpa* provides aloin A/B which then can undergo oxidative hydrolysis to yield aloe-emodin and rhein via oxidized aloe-emodin. These anthrones are showed remarkable antiprotozoal activity. Aloe-emodin can induce cell death in promastigotes of *Leishmania sp* [167]. There are other compounds in latex of *A. macrocarpa* which is anthraquinone. Anthraquinone possessed it leishmanial activity by intercalating DNA of the parasites as well as participated in oxidative stress. Anthraquinone intercalated with nucleophiles in cell and involved in redox reaction. Subsequently, reactive oxygen species (ROS) are generated and oxidative stress occurs. Aloe-emodin and rhein are potentially used in synthesized antileishmanial drug since they are effectively against *Leishmania dovani* and *Leishmania aethiopica* promastigotes and axenic amastigotes. They also can be used to treat malaria[168]. *Aloe ghibensis* are used to treat skin problems, malaria and for wounds healing. Similar to *A. marcrocarpa,* it also containing aloin A/B as well as 7-hydroxyaloin A/B which also have significant antileishmanial activity against *Leishmania dovani* and *Leishmania aethiopica* promastigotes[169].

Peruvian used *H. sucuuba* to make their traditional remedy against leishmania since latex of *H. sucuuba* possessed remarkable antileishmanial properties. It is specifically against intracellular amastigotes of *Leishmania amazonensis*. Two spirolactone iridoids, isoplumericin, and plumericin can be isolated from the latex of *H. sucuuba* and these spirolactone iridoids are responsible for antileishmanial activity. Plumericin is capable of reducing the macrophage infection[170]. Triterpenoids α-amyrin which found in Sambucol also can be found in *H. sucuuba* latex. Triterpenoids α-amyrin play a role in inducing production of TNF- α[171]. *H. sucuuba* also possessed antiprotozoal activity against *Plasmodium falciparum* which is the causative agent of malaria. It scavenges nitric oxide to inhibit nitric oxide synthesis and reduces the concentration of nitric oxide. Thus, it disrupted the pathogenesis of malaria. Lectins isolated from latex of *Synadenium carinatum* also effectively against *L. amazonesis* amastigotes. It activates nitric oxide independent pathway to induced apoptosis instead of induced nitric oxide production which is related to pathogenesis of *leishmania*. Subsequently, the number of intracellular *Leishmania* reduced[172].

C. procera exhibited schizonticidal activity against *P. falciparum.* Anti-plasmodial and inhibitory effects against malaria are due to acetogenins presence in the latex of *C. procera*. Latex of *C. procera* are effective in controlling *Culex pipiens* since it can act as larvicidal agents[173]. *E. Hirta* demonstrated anti-malarial activity since it contains various bioactive constituents such as flavonol glycosides afzelin, quercetin, and myricitrin. These components possess antiplasmodial activity so they potentially act as inhibitors on proliferation of *P. falciparum.*

Antileishmanial effects of *Galipea longiflora* are due to it containing quinoline alkaloids. Chimanine B, chimanine D and 2-n-propylquinoline significantly reduced the lesion and loads of parasites when administered orally. 2-n-propylquinoline even inhibits p-glycoprotein activity in the intestine. Hence, it can be used in synthesized antileishmanial drugs against multiple drug resistance leishmania associated with kala-azar. Apart from that, other quinoline alkaloids included 2-(3,4-dimethoxyphenylethyl) quinoline, cusparine and furanoquinoline alkaloid skimmianine. Furanoquinoline alkaloid skimmianine acts by inhibiting adenine phosphoribosyltransferase, a parasite enzyme in *Leishmania spp.* Quinoline alkaloids also exert inhibitory effects on epimastigotes of *Trypanosoma cruzi* which caused Chagas disease[174].

Conclusion

Plant latex is an essential source of natural second metabolites which apply in various fields such as medical, rubber industry and nanotechnology. They also inhibit the growth of bacteria, fungi, protozoan and cancer cell lines. It also is a good antioxidant and anti-inflammatory as well as analgesic agents. It induced cell death thus demonstrated anticancer activity. Anti-inflammatory activities are acted by involvement in the initial phase or late phase. Antioxidants activity of latex even enhanced the effectiveness of anticancer properties. Some of the latex are antimalarial, antileishmanial and anti-plasmodial. Plant latex possesses these properties due to it containing various bioactive compounds. For example, alkaloids, terpenoids, protease, lignin, flavonoids, cardiac glycosides, anthrone and saponins. Definitely, plant latex is a fundamental source for industry since it is low cost and easy to be manufactured into products which are waterproof and highly flexible. Our daily life is commonly in touch with rubber such as footwear, rubber band, wire, insulating layer and tyres. It even plays a vital role in medical fields such as medical products and antibiotics for bacterial infection. Apart from that, nanocarriers for drug delivery also can be synthesized easily to improve the efficacy of drug delivery systems. Plant latex also is a potent anticancer drug and it may act synergic with other anticancer drugs. Plant latex are eco-friendly because it is biodegradable and easy to recycle. Hence, products manufactured from plant latex are safer. However, toxicity of plant latex to the human body must be determined properly since there are some plant latex which are highly toxic.

Availability of data and materials

The datasets used and/or analysed during the present study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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