REVIEW PAPER

Volume 3, Issue 1, pp 215-238, June 2021

ACHIEVERS JOURNAL OF SCIENTIFIC RESEARCH

Open Access Publications of Achievers University, Owo

Available Online at www.achieversscience journal.org

Effect of Some Selected Plants in the Treatment of Viral Infection

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Submitted: April 10, 2021, Revised: April 30, 2021, Accepted: June 3, 2021, Published: June 28, 2021

ABSTRACT

Medicinal plants have posed as natural resources of compounds with pharmacological and nutritional properties aiding humans to prevent and treat diseases. These plants also have therapeutic properties and exert beneficial pharmacological effect on man and animal as curative medicine. Thus, necessitating the need to select some plants such as: Turmeric (*Curcuma longa*), Bitter Kola (*Garcinia kola Heckel*), *Mimosa pudica*, *Ganoderma lucidium*, *Persea americana*, Ginger (*Zingiber officinale*), *Moringa Oleifera and* grape in the treatment of viral infection. The study majorly review literatures on those selected plants in the treatment of viral infection due to their availability, affordability and current integration of herbal medicine into modern health care plan to proffer scientific solution to health care problem through the use of medicinal plant. Therefore, the active ingredients of these selected plants can be good candidates in the treatment of viral diseases.

KEYWORDS: Avocado; Bitter Kola; Drumstick Tree; Ginger; the Reishi Mushroom; Tumeric.

1. Introduction

Turmeric (*Curcuma longa*) is a perennial herb and member of the *Zingiberaceae* (ginger) family and is cultivated extensively in Asia mostly in India and China. The rhizome, the portion of the plant used medicinally, yields a yellow powder (Louay, 2014). In addition to *Curcuma longa L.*, the genus turmeric contains about 30 other species. The name Curcuma is derived from the Arabic word "turmeric" which means yellow. In Sanskrit, turmeric has 55 different names associated with its religious and medical use (Ravindran, 2007; Daria *et al.*, 2017). Turmeric is a plant distributed throughout tropical and subtropical regions of the world. It is widely cultivated in Asian countries, mainly in China and India. The plant measures up to 1 m high with a short stem, it has oblong, pointed leaves and funnel-shaped yellow flowers. The rhizome, the portion of the plant used medicinally, is usually boiled, cleaned, and dried, yielding a yellow powder and the dried Curcuma longa is the source of the spice turmeric, the ingredient that gives curry powder its characteristic yellow colour (Nasri *et al* 2014; Roshan and Gaur, 2017).

However, Turmeric is used extensively in foods for its flavour and colour, as well as having a long tradition use in the Chinese, Ayurveda and in Asian countries such as India, Bangladesh and Pakistan systems of medicine; India has a rich history of using plants for medicinal purposes (Roshan and Gaur, 2017). It is used in the textile and pharmaceutical industries and in Hindu

religious ceremonies in one form or another. Current traditional Indian medicine uses it for biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism, and sinusitis. The old Hindu texts have described it as an aromatic stimulant and carminative. Powder of turmeric mixed with slaked lime is a household remedy for the treatment of sprains and swelling caused by injury, applied locally over the affected area. Safety evaluation studies indicate that both turmeric and curcumin are well tolerated at a very high dose without any toxic effects. Thus, both turmeric and curcumin have the potential for the development of modern medicine for the treatment of various diseases (Roshan and Gaur, 2017).

Furthermore, various parts of these plant species have been used either raw or cooked as vegetables in many Asian countries (Devi *et al.,* 2014). They also considered as nutritionally rich foods because Curcuma plants are a rich source of starch, carbohydrates, proteins, fats, vitamins, and minerals (Roshan and Gaur, 2017; Kaliyadasa and Samarasinghe, 2019). Curcuma plants have been shown to contain various bioactive molecules, which possesses many pharmacological properties such as; anti-inflammatory (Sikha *et al.,* 2015), antimicrobial (Jagtap, 2015), hypocholestraemic (Jagtap, 2015), antirheumatic (Abdel-Lateef *et al.,* 2016), antiviral (Pant *et al.,* 2013), antifibrotic (Pant *et al.,* 2014); antihepatotoxic (Jagtap, 2015); antidiabetic (Sikha *et al.,* 2014); antinociceptive (Ramasree and Indira, 2006); anticancerous (Pawar *et al.,* 2011); gastroprotective properties (Jeon *et al.,* 2015) and beneficial effects on cardiovascular diseases (Nithya and Jayashree, 2017). Plants belonging to the genus Curcuma are gaining importance all over the world and subjected for many investigation and exploration in recent years due to its promising potentials and wide range of usage. Therefore, a proper morphological and physicochemical identification is necessary, but not systematically studied yet. This review intends to provide a comprehensive insight into the morphology, phytochemistry and pharmacology of the genus Curcuma (Kaliyadasa and Samarasinghe, 2019).

2. Turmeric (*Curcuma longa*)

Morphological characteristics of turmeric (*curcuma longa*)

Many researchers have been studied the morphological characteristics of different species in genus Curcuma. When one considers the Morphology, the genus Curcuma is highly variable in taxonomically important traits. Four tribes in family Zingiberaceae were recognized namely, Globbeae, Hedychieae, Alpinieae and Zingibereae based on morphological features like number of locules and placentation in the ovary, development of staminodes, modifications of the fertile anther, and rhizome-shoot-leaf orientation (Kress *et al.*, 2002; Kaliyadasa and Samarasinghe, 2019), where Curcuma is belongs to Zingibereae. Commonly the rhizomes of Curcuma are branched, fleshy and aromatic (Revathi and Malathy, 2013; Kaliyadasa and Samarasinghe, 2019). Roots attached to the rhizome often bear conical or ellipsoid tubers (Kaliyadasa and Samarasinghe, 2019). Basal leaf blades are normally broad, lanceolate or oblong or rarely linear in shape. Flowers contain a single versatile anther and spiral bract with large compound spike inflorescence is a prominent characteristic when recognizing the genus Curcuma (Dung *et al.,* 1998; Kaliyadasa and Samarasinghe, 2019). The terminal bracts form a sterile cluster is very long and often brightly coloured. It has two distinct flowering times. Early flowering species develop flowers laterally from rhizomes before the development of leafy shoots and late flowering species usually developed terminally from the leafy shoots The plants are normally 50 to 200 cm in height. Curcuma species are mostly triploid and reproduce asexually by rhizomes and they do not produce seeds (Kaliyadasa and Samarasinghe, 2019). Morphology of the different early flowering Curcumas lead to identification problems because they exhibit large intra- and inter specific morphological variations. C. longa rhizome is medium sized, aromatic and conical in shape. The internal colour of the rhizome is deep orange-yellow (Abdel-Lateef *et al.,* 2016; Kaliyadasa and Samarasinghe, 2019). They are native to Southeast Asia, southern China, the Indian Subcontinent, New Guinea and Northern Australia and naturally found

in some warm regions of the world such as tropical Africa, Central America, Florida, and various islands of the Pacific, Indian and Atlantic Oceans. It has cylindrical and branched sessile tubers. Leaf lamina is oblong-lanceolte with wavy margins and short ligules. Inflorescence is in the middle. The peduncle concealed within the leaf sheaths Spike has a distinct white coma and bracts are pale green. Corolla tubes of the large flowers are white in colour with unequal lobes. Labellum is light yellow in color with a median dark yellow band. Lateral staminodes are linear and anthers are spured (Kaliyadasa and Samarasinghe, 2019).

3. Phytochemicals of turmeric (*curcuma longa*)

The rhizomes of the Curcuma species are the most commonly used part for chemical extractions. Nonvolatile curcuminoids and volatile oils are the main active components of the rhizome. Curcumin, demethoxycurcumin and bisdemethoxycurcumin are the major curcuminoids. They are nontoxic polyphenolic derivatives of curcumin. Sesquiterpenoids and monoterpenoids are identified as the major components in Curcuma oil (Kaliyadasa and Samarasinghe, 2019).

C. longa is the major species subjected to many studies. It contains protein (6.3%), fat (5.1%), minerals (3.5%) and carbohydrates (69.4%) and its essential oil (5.8%) is obtained by steam distillation of rhizomes contains a-phellandrene, sabinene, cineol, borneol, zingiberene and sesquiterpines (Kaliyadasa and Samarasinghe, 2019). Curcumin (diferuloylmethane) is the compound responsible for the yellow colour, and it comprises of curcumin I (94%), curcumin II (6%) and curcumin III (0.3%), then the chemotypes in the turmeric vary widely. There are hundreds of compounds identified from the turmeric essential oils such as; ar-turmerone, α-turmerone, and β-turmerone, followed by notable amounts of α-zingiberene, curlone, ar-curcumene, α-santalene, santalenone, βsesquiphellandrene, (Z)-β-ocimene, β-bisabolene, βcaryophyllene, α-phellandrene, (Z)-β-farnesene etc (Kaliyadasa and Samarasinghe, 2019). There is a significant variation in between the essential oils obtained from fresh and dry rhizomes of Curcuma longa. The Oil extracted from rhizome of C. zedoaria is mainly composed of sesquiterpenoids and monoterpenoids. Essential oils in Curcuma aeruginosa is usually composed of relatively equal amounts of monoterpenes and sesquiterpenes such as; 8,9-dehydro-9-formyl-cycloisolongifolene (35.3%), dihydrocostunolide (22.5%) , germacrone (23.5%), curzerenone (11.8%) dehydrocurdione (27.6%), curcumenol (15.1%), 1,8-cineole (22.7%), germacrone (17.7%) Generally, monoterpenes are predominated (80–88%) in rhizomes of Curcuma zanthorrhiza (Nayak *et al*., 2017; Kaliyadasa and Samarasinghe, 2019)).

The major constituents in Curcuma aromatica rhizome consisted with 8,9-dehydro-9- formyl-cycloisolongifolene (2.7- 36.8%), germacrone (4.3-16.5%), ar-turmerone (2.5- 17.7%), turmerone (2.6–18.4%), curdione (50.6%), camphor (18.8-32.3%), xanthorrhizol (26.3%), arcurcumene (19.5%), di-epi-α-cedrene (16.5%), curcumol (35.8%), and 1,8-cineole (12.2%) (Kaliyadasa and Samarasinghe, 2019). Curcuma phaeocaulis rhizome has 8,9-dehydro-9-formylcycloisolongifolene (15.6-46.2%), germacrone (8.9- 21.2%), and curlone (0.8-20.2%) as the main constituents. Curcuma caesia composed mainly of 1,8-cineole (30.1%) followed by camphor, arcurcumene, and camphene(Zeng *et al.*, 2007; Kaliyadasa and Samarasinghe, 2019). However, different Curcuma species produce a wide variety of volatile sesquiterpenes, monoterpenes, and other aromatic compounds (Devi *et al.*, 2014; Kaliyadasa and Samarasinghe, 2019). There is a significant variation in composition of Curcuma essential oils. Genotype, variety, geographical location, climate, season, cultivation practices, fertilizer application, stress during growth or maturity, harvesting time, stage of maturity, storage, extraction, and analysis methods will greatly determine different oil chemical profiles .

Though, some of the variation could be due to misidentification of the plant species or some of the components (Abdel-Lateef *et al.*, 2016; Kaliyadasa and Samarasinghe, 2019)

4. Pharmacological Action OfTurmeric (*curcuma longa*)

Phytochemicals of Curcuma species possesses a wide variety of pharmacological properties,

including antiinflammatory (Sikha *et al.,* 2015), anticancerous, antiproliferative, hypocholesterolemic , antidiabetic, antihepatotoxic, antidiarrheal, antimicrobial and insecticidal activities (Jagtap, 2015). Curcuma oils are also known to enhance immune function, promote blood circulation, accelerate toxin elimination, and stimulate digestion. C. longa and C. zedoaria are the most widely studied species of genus Curcuma (Abdel-Lateef *et al.*, 2016).

5. Specific mode of action on virus

Lack of effective therapeutics for most of the viral diseases, emergence of antiviral drug resistance, and high cost of some antiviral therapies necessitate findings of new effective antiviral compounds (Lemoine *et al.,* 2013). In addition the existing antiviral therapies are not always well-tolerated and are quite effective as well as satisfactory. Therefore, increasing requirement for antiviral substances will be more highlighted. Plants are equally rich source of phytochemicals with different biological activities including the antiviral activities which are the interest of scientists (Moghadamtousi *et al.,* 2013). It has been demonstrated that curcumin as a plant derivative has a wide range of antiviral activity against different viruses in which Inosine monophosphate dehydrogenase (IMPDH) enzyme by rate-limiting activity in the de novo synthesis of guanine nucleotides is suggested as a therapeutic target for antiviral and anticancer compounds and among the 15 different polyphenols, curcumin through inhibitory activity against IMPDH effect in either noncompetitive or competitive manner which suggested it as a potent antiviral compound via this process (Dairaku, 2010). The study of different bioconjugates of curcumin, namely, di-O-tryptophanylphenylalanine curcumin, di-O-decanoyl curcumin, di-O-pamitoyl curcumin, di-Obis-(γ,γ)folyl curcumin, C4 -ethyl-O-γ-folyl curcumin, and 4-O-ethyl-O-γ-folyl curcumin, against variety of viruses including parainfluenza virus type 3 (PIV-3), feline infectious peritonitis virus (FIPV), vesicular stomatitis virus (VSV), herpes simplex virus (HSV), flock house virus (FHV), and respiratory syncytial virus (RSV) assessed by MTT test showed the potent antiviral activity of curcumin and its bioconjugates against different viral pathogens. Also, di-O tryptophanylphenylalanine curcumin and di-O-decanoyl curcumin revealed remarkable antiviral activity against VSV and FIPV/FHV with EC50 values of 0.011 μM and 0.029 μM, respectively. However, bioconjugates did not exhibit significant antiviral activity against IIIB and ROD strains of type 1 human immunodeficiency virus (HIV-1) in MT-4 cells (Singh *et al.,* 2010).

Viral long terminal repeat (LTR) has a critical role in transcription of type 1 human immunodeficiency virus (HIV1) provirus. Inhibition of LTR activity can be a possible pathway for antiviral drug candidates in order to block HIV1 replication. Curcumin proved to be an effective compound to inhibit the HIV-1 LTR-directed gene expression without having any major effects on cell viability (Moghadamtousi et al., 2014). Curcumin and its derivatives, namely, reduced curcumin, allyl-curcumin, and tocopheryl-curcumin, revealed 70% to 85% inhibition in Tat protein transactivation of HIV-1 LTR measured by β-galactosidase activities of HeLa cells which in HIV-1 LTR was fused to the indictor of lacZ gene. Tocopheryl-curcumin demonstrated the most inhibition activity with 70% inhibition at 1 nM compared to 35% inhibition of curcumin at this concentration. Furthermore, curcumin inhibited the acetylation of Tat protein of HIV significantly by p300 associated with suppression of HIV-1 multiplication as well as by targeting the acetyltransferase proteins of p300/CREB binding protein (CBP) which can be a potent compound for combinatorial HIV therapeutics (Moghadamtousi et al., 2014). However, Curcumin has been found to be an inhibitor of HIV-1 and HIV-2 protease with IC50 of 100 μM and 250 μM, respectively. The curcumin boron complexes exhibited noteworthy inhibition reduced to the IC50 value of 6 μM with time-dependent activity. The elevated affinity of boron derivatives of curcumin is possibly associated with the attachment of the orthogonal domains of the compound in intersecting sites within the substrate-binding cavity of the protease and Integrase which is another essential enzyme for HIV-1 replication was found to be inhibited by curcumin with IC50 value of 40 μM whereby, the Inhibition of deletion mutant of integrase containing only amino acids 50–212

indicating that curcumin possibly interacts with catalytic core of the enzyme. The study of energy minimization and the structural analogs of curcumin elicited that an intramolecular stacking of two phenyl rings of curcumin is possibly responsible for anti-integrase activity via bringing the hydroxyl groups into close proximity. However, rosmarinic acid and dicaffeoyl methane as two curcumin analogs showed noteworthy inhibitory activity against integrase of HIV-1 with IC50 values less than 10 μM with the slow rate of binding to the enzyme assessed by kinetic studies (Mazumder *et al.,* 1997; Moghadamtousi et al., 2014). Though, through a clinical trial investigation on curcumin as an anti-HIV compound in 40 patients in eight weeks it was shown that there is no reduction in viral load or elevation in CD4 counts. But patients claimed that they preferred to take the curcumin in order to tolerate the minor gastrointestinal sufferings and feel better. This demonstrated that clinical trials can possibly show up with the results completely different from in vitro studies. The clinical trial of clear liquid soap containing 0.5% w/v ethanol extract of C. longa rhizome on HIV patients reduced the wound infections and 100% decrease in itching symptom and it also affected the abscess to convert to dryness scabs (78.6%) within 2 weeks (Ungphaiboon *et al.,* 2005)

6. Turmeric (*curcuma longa*) action on influenza virus

Curcumin has showed the anti-influenza activity against influenza viruses PR8, H1N1, and H6N1 and the results showed more than 90% reduction in virus yield in cell culture using 30 μM of curcumin. The plaque reduction test elicited the approximate EC50 of 0.47 μM for curcumin against influenza viruses (Chen *et al.,* 2010). In H1N1 and also H6N1 subtypes, the inhibition of haemagglutinin interaction reflected the direct effect of curcumin on infectivity of viral particles and this has proved by time of drug addiction experiment. Furthermore, unlike amantadine, viruses developed no resistance to curcumin. The methoxyl derivatives of curcumin also did not show noteworthy role in the haemagglutination (Chen *et al.,* 2010). These results proved the significant potential of curcumin for inhibition of influenza.

7. Turmeric (*curcuma longa*) action on herps virus

In vitro study of curcumin and its derivatives, namely, gallium-curcumin and Cu-curcumin, exhibited remarkable antiviral activity against herpes simplex virus type 1 (HSV-1) in cell culture with IC50 values of 33.0 microg/mL, 13.9 microg/mL, and 23.1 microg/mL, respectively. The 50% cytotoxic concentration (CC50) of the respective compounds on Vero cell line showed to be 484.2 μg/mL, 255.8 μg/mL, and 326.6 μg/mL, respectively (Zandi *et al.,* 2010). Curcumin considerably decreased the immediate early (IE) gene expression and infectivity of HSV-1 in cell culture assays. Curcumin has an effect on recruitment of RNA polymerase II to IE gene promoters through mediation of viral transactivator protein VP16, by an independent process of p300/CBP histone acetyl transferase effect. In vitro replication of HSV-2 could be decreased by curcumin with ED50 value of 0.32 mg/mL. Moreover, an in vivo study on mouse model with intravaginal HSV-2 challenge showed significant protection against HSV-2 infection due to administration of curcumin. This study showed that curcumin can be a good candidate for developing the antiviral products used intravaginally by women for protection against sexually transmitted herpes virus infection. Actually, a metallo-herbal complex of curcumin with copper (Cu2+) demonstrated microbicidal effect which could be for further studies of vaginal gel with antiviral activity (Chauhan *et al.,* 2013).

8. Turmeric (*curcuma longa*) action on hepatitis b virus

Liver diseases associated with viral infections are major pandemics and the fact that hepatitis B virus (HBV) elevates the possibility for the hepatocellular carcinoma (HCC) development of some 100-fold and 695.900 deaths occurred due to liver cirrhosis and HCC worldwide in 2008 makes the need to find new antivirals against hepatitis viruses (Jemal *et al.,* 2011). The study of antiviral effect of aqueous extract of Curcuma longa rhizoma against HBV in HepG 2.2.15 cells containing HBV genomes showed repression of HBsAg secretion from liver cells

without any cytotoxic effect. It also suppressed the HBV particles production and the rate of mRNA production of HBV on infected cells. The Curcuma longa extract suppressed HBV replication by increasing the rate of p53 protein through enhancing the stability of the protein as well as transactivating the transcription of p53 gene. It was understood that the extract has suppressed HBV enhancer I and X promoter leading to repression of HBx gene transcription by affecting p53 (Jemal *et al.,* 2011). In vitro investigation of the antiviral activity of curcumin Huh7 replicon cells expressing the hepatitis C virus (HCV) indicated that curcumin can be a potent anti-HCV compound due to the results which shows the decrease in HCV gene expression and replication through suppressing the AktSREBP-1 pathway. In addition, the mixture of curcumin and IFNα as the known anti-HCV therapy induced profound inhibitory activity on HCV replication and demonstrated that curcumin can be possibly used as a complementary therapy for HCV (Kim *et al.,* 2010).

9. Bitter Kola as an Antiviral Agent

Bitter Kola (Garcinia kola Heckel), a genus belonging to the diverse pantropical family of Clusiaceae which consists of mainly woody perennials, trees, shrubs, and lianas divided into 18 genera. Among them are Calophyllum, Clusia, and Garcinia which is the most popular important fruit and medical tree species. It's commonly known to be distinct bitter taste-hence is called bitter kola and as well refers to has "male kola" because of its claimed aphrodisiac activity zand plays an important role in African ethnomedicine and traditional ceremonies (Gustafsson, 2018). The trees are naturally found in humid tropical forests of West and Central Africa, where the local population usually harvest the fruits. However, in some regions, farmers plant and manage the trees in their homegardens or agroforests outside natural forests and its seeds are amongst the most-traded NTFPs in West and Central Africa and the species is sometimes referred to as a "wonder plant" because each of its parts can be used as medicine (Dranca and Oroian, 2016). The most valued product is the seeds, commonly chewed by both rural and urban populations to avoid and treat gastric problems or simply for their typical astringent taste and the kernel contains a wide range of useful phytochemicals, e.g., high contents of tannins and flavonoids and among these compounds, the biflavonoid kolaviron complex is the most discussed due to its reputedly holds neuroprotective, anti-inflammatory, antimicrobial, anti-malarial, wound healing properties and many other assets favorable to human health (Stevens, 2018). Kolaviron also as therapeutic potential in the treatment of benign prostatic hyperplasia, neurodegenerative diseases such multiple sclerosis and acquired immunodeficiency syndrome (AIDS). Meanwhile the seed extract was able to stop growth of Ebola virus in laboratory trials (Nworu *et al.,* 2008;Kalu*et al.,* 2016;Omotoso *et al.,* 2018).

10. Phytochemicals of bitter kola (*garcinia kola hl*)

The most abundant phytochemicals in G. kola seeds are flavonoids. Presence of saponins, tannins, phenols, glycosides, and alkaloids has also been confirmed by various authors. Even though anti-nutrients such as oxalate and phytate were detected, the seeds are safe for consumption and there are no reports on harmful overdosing so far (Konziase, 2015). Flavonoids, compounds of low molecular weight, are known as natural antioxidants, having an ability to scavenge free radicals and transform them into harmless molecules as well as to impact various aspects of the immune cell activation for human body. These compounds play a useful role in protecting the central nervous system against oxidative, excitotoxic stresses (Nworu *et al.,* 2008; Ijomone *et al.,* 2012) and work as anti-tumor (benign, melanoma) agents (Altemimi *et al.,* 2017). One of the most studied and discussed components in G. kola seeds is the kolaviron biflavonoid complex (KV). This complex further consists of biflavanones GB1, GB2, and kolaflavanone (Tchimene *et al.,* 2015).

11. General mode of action bitter kola

Kolaviron (KV) possesses antinociceptive (sedative) and anti-inflammatory activities, both centrally and peripherally, which justifies its folkloric use to relieve pain and inflammation. The anti-

inflammatory effect of KV and its components was observed in carrageenan-induced paw edema test (Nwaehujo et al., 2015). Moreover, Abarikwu (2015), revealed that KV can block signaling pathways implicated in lipopolysaccharide induced inflammatory gene expression in RAW 264.7 macrophage cell line and In another experiment carried out by Farombi *et al.*, (2018) , KV extended the lifespan of the common fruit fly (Drosophila melanogaster) by preventing oxidative stress and inflammation in the species. The KV extracts significantly decreased locomotion, grooming, and rearing frequencies of male Swiss mice indicating a central depressant effect of the complex. As well in another finding it also shows that KV could prevent neuro-destructive effects of methamphetamine on hippocampal neurons, affording some protection to the hippocampus too (Ijomone *et al.*, 2012) and this is due to its abilities to combat oxidative and inflammatory damage induced by cuprizone, KV showed therapeutic potential against degenerative changes associated with demyelination and neurotoxicity. This finding might be later used in treatment for a multiple sclerosis (Omotoso *et al.*, 2018). Additionally, KV can be a clinically viable agent against ischemia/reperfusion injuries (Odukanmi *et al.*, 2018)

12. Anitviral Activity of Bitter Kola (*Garcinia Kola Heckel*)

Antiviral properties are found in Garcinia family in which various species in the Garcinia genus have been reported to possess antiviral properties. These species include Garcinia livingstonei, Garcinia ovalifolia (Gustafson *et al.*, 1992), and Garcinia mangosteen (Chen *et al.*, 1996), among others. The compounds responsible for the antiviral properties have been identified as guttiferones. Guttiferones are polyisoprenylated benzophenone derivatives that inhibit by cytopathic effects the activity of the virus responsible for HIV infection (Gustafson *et al.*, 1992). Most polyprenylated benzophenones isolated from these plants also contain carbonyl, hydroxyl and other polar groups. Perhaps the most cited naturally-occurring, Garcinia-derived benzophenone in the literature is camboginol, also a synonym for garcinol. Garcinol is a polyisoprenylated benzophenone which has been- recovered from Garcinia assigu, (Ito *et al.*, 2003) Garcinia indica (Hong *et al.*, 2007), Garcinia purpurea (Matsumoto *et al.*, 2003), Garcinia banacana (Rukachaisirikul *et al.*, 2005), Moronobea coccinea (Marti *et al.*, 2008), and Allenblackia monticola (Lenta *et al.*, 2007) and assayed for 7 cytotoxicity as well as anti-bacterial, anti-viral, and anti-parasitic activities. Garcinol has the same or even very similar structural to that of Guttiferone F (Gustafson *et al.*, 1992) and the names are said to be used interchangeable (Fuller *et al.*, 1999). Guttiferone and related benzophenone antiviral compounds have been reported to be isolated from Garcinia kola and other Garcinia spp. and they contain a number of valuable biological active compounds. However, relatively few studies have been reported describing the design and performance of Garcinia derived formulations and drug delivery systems on its proposed antiviral properties.

13. *Mimosa pudica*as an Antiviral Agent

Mimosa pudica (*M. pudica*, Linn) is an annual or perennial herb belonging to family Mimosaceae, common plant in moist waste ground distributed throughout in India locality, lawns, open plantation and weedy thickets, in which the leaves close and the petiole hangs down in response to certain stressors such as a wound, wind, vibration, touch, hot or cold stimulus, drought or change in illumination. Seismonastic movements such as response to touch, appear to be regulated by electrical and chemical signal transduction, spreading the stimulus throughout the plant (Alexander *et al.*, 2010). *M. pudica*, is commonly known as 'lajjalu' in Hindi, 'touch-me-not' in English and 'thottalsenungi' in Tamil. *M. pudica* has been reported to contain mimosin (an alkaloid), free amino acids, beta-sitosterol, linoleic acid and oleic acid (Kokane, 2009). A diffuse prickly under shrub, is about 45-90 cm in height. Leaves bipinnately compound, pinnate 2-4 delicately arranged with 10-20 pairs of leaflets, rachis clothed with ascending bristles. The known medicinal properties of *M. pudica* are antivenom properties, arresting bleeding, skin diseases, wound healing activity, alleviating headache, insomnia, diarrhea, dysentery, fever, piles, fistula, anticonvulsant activity, anti-hyperglycemic and hepato-protective activity and antiviral activity

(Parimala and Manoharan, 2009; Rekha *et al.,* 2009; Malayan *et al.,* 2013).

Mimosa plant has a history of use for the treatment of various ailments and the most commonly used plant part for this purpose is the root, but its flowers bark and fruit can as well be utilized. Meanwhile, several research works have been carried out to study the phytochemical components of *Mimosa pudica* and its efficacy against some microbial effect (antimicrobial activity),

14. Phytochemical properties of *Mimosa pudica*

According to Malayan *et al.,* (2013), phytochemical compound present in Mimosa Pudica arealkaloids, flavonoids, saponins, carbohydrates, phenols, steroids, tannins, diterpenes and glycosides and using (GC–MS) gas chromatography–mass spectroscopy, study shows the present of several compounds which was found to be most predominant. One of the compounds known as 2-[2-methyl-5-nitro-imidazol-1-yl]-N-phenethyl-acetamide (chemical formula C14H16N4O3; molecular weight 288.30184 kDa) showed a peak area with RT of 13.85. This compound was most abundant in *M. pudica* extract and could be responsible for the observed antiviral activity.

15. General mode of action*M. pudica*

Wound healing activity: The *M. pudica* shoot methanolic extract, M. pudica root methanolic extract showed very good wound healing activity (Kannan *et al.,* 2009). The methanolic extract exhibited good wound healing activity probably due to presence of phenols constituents (Volkov *et al.,* 2008).

16. Specific mode of action on virus

Using the experiment done by Malayan *et al.,* (2013), on Anti-mumps virus activity by extracts of *Mimosa pudica* to discuss and demonstrate the mode of action of this plant on virus. Its report shows that *M. pudica* extract possesses varied medicinal benefits, including anti-hepatitis B activity, for its effectiveness against MuV (mumps virus). Because standard strains of MuV were not available for testing, but a strains which were isolated from patients with acute mumps infection, who had also tested positive for anti-mumps IgM antibody. Upon genotypic characterization, it was found that these strains belonged to genotype C (first report in India) and a Sequences were submitted to GenBank and phylogenetic analyses was done (GenBank accession no. JX392385, JX392386, JX894238, JX894239, JX894240). However, different concentration of *M. pudica* methanolic extracts showed that 150 µg/ml of M. pudica extracts inhibited viral replication and prevented about 95 % of CPE development. The continuous presence of the extracts in the cell culture medium is apparently essential for continuous protection of Vero cells against viral CPE development. This observation was based on absence of CPE, as well as the inhibition of virus replication, but the toxicity of the extract was also carried out using MTT assay according to Malayan *et al.,* (2013) and its experimental reports shows that the extracts were non-toxic up to 2 mg/ml concentration and cells had 100 % viability. It has also been widely observed and accepted that the medicinal value of plants lies in the bioactive phytocomponents present in the plants. The active principle of the phyto components of *M. pudica* were studied and the antiviral activity of the plant extract was tested against MuV in different concentrations of the extract to assess the most effective concentrations and it was discovered that apart from the common phytocomponents found in the plant other compound that make it antiviral against this MuV is 2-[2-Methyl-5-nitro-imidazol-1-yl]-N-phenethyl-acetamide (chemical formula $C_{14}H_{16}N_4O_3$; molecular weight 288.30184 kDa) showed a peak area with RT of 13.85 this was the most abundant in *M. pudica* extraction but other compound include: Cholan-24-oic acid, 3, 12-dihydroxy-, methyl ester, [3a, 5a, 12a]-(chemical formula $C_{27}H_{44}O_5$; molecular weight 448.64kDa) with RT of 15.07, Propanoic acid, 2-(3-acetoxy-4,4,14-trimethylandrost-8-en-17-yl)- (chemical formula $C_{27}H_{42}O_4$; molecular weight 430.61998kDa) with RT of 11.43

17. *Ganoderma Lucidium*as An Antiviral Agent

Ganoderma Lucium also called lingzhi or reishi mushroom is a polypore fungus is red-varnished,

kidney-shaped cap and peripherally inserted stem gives it a distinct fan-like appearance. When fresh, the *Ganoderma lucidium* is soft, cork-like, and flat. It lacks gills on its underside, and instead releases its spores via fine pores. Depending on the age, the pores on its underside may be white or brown (Arora and David, 1986). *Ganoderma lucidum* and its close relative, *Ganoderma tsugae*, grow in the northern Eastern Hemlock forests. These two species of bracket fungus have a worldwide distribution in both tropical and temperate geographical regions, growing as aparasite or saprotroph on a wide variety of trees. Similar species of *Ganoderma* have been found growing in the amazon (Hobbs and christopher, 2002). Ganoderma lucidium is used for cancer, aging, boosting the immune system to prevent or treat infections, and for many other reasons, but there is no good scientific evidence to support these uses (Jin *et al*., 2012).

The family Ganodermetaceae Taxonomy describes polyphore basidomycetous fungi having a doubled wall basidospore in all 219 species within the family have been assigned to the genius Ganoderma lucidium (Monclavo, 2000) owing to its irregular distribution in the wild and increasing demand of Ganoderma lucidium as a medicinal herb attemps were made to cultivate the mushrrom (Chang *et al*., 2008) Different member of Ganoderma lucidium needs different conditions for growth and cultivation and the different types are favoured in different geographical regions in South china black Ganoderma lucidium is popular and red Ganoderma lucidium is preferred in japan, Ganoderma lucidium they thrive under hot and humid conditions and many wild varieties are found in the subtropical regions of the orient since the early 1970's Ganoderma lucidium has become a major source of mushroom artificial cultivation of Ganoderma lucidium had been achieved using substrates such as grain, sawdust, woodlogs (Chang and Buswell, 1999).

Ganoderma lucidum has anti-oxidative effects when supplemented. It also has a therapeutic effect on insulin resistance, reduces the risk of prostate cancer, and can help treat a variety of conditions associated with metabolic syndrome. Ganoderma lucidium is well known for its anti-cancer effects. It is able to activate natural killer cells, increasing their activity and the body's ability to fight tumors as well serve as a Supplement by reducing the chances of metastasis, which is when cancer spreads to another part of the body. *Ganoderma lucidum* has a variety of mechanisms, but they are focused on moderating the immune system (Yuen andLai, 2011). The lingzi mushroom is able to reduce immune system activity when the system is overstimulated, and bolster the immune system when it is weakened. In general, *Ganoderma lucidum* increases the amount of active immune system cells. *Ganoderma lucidium* is usually well-tolerated with few significant side effects. *Ganoderma lucidium* also contains a substance that may act like a blood thinner, potentially triggering bloody stools, nosebleeds, and easy bruising. *Ganoderma lucidium* should be avoided in people with bleeding disorders or liver disease. It should not be used if you are taking anticoagulants like warfarin or are scheduled to have surgery as it may increase the risk of bleeding. Ganoderma Lucidium may also cause your blood pressure to drop and should be avoided if you are taking antihypertensive medications. Doing so may lead to hypotension (low blood pressure), triggering dizziness, fatigue, nausea, and blurry vision.Due to the lack of safety research, *Ganderma Lucidium* should be avoided in children, pregnant women, and breastfeeding mothers (Klupp *et al*., 2015).The popular edible mushroom *Ganoderma lucidum* has been widely used for the general promotion of health and longevity in Asian countries. The dried powder of *Ganoderma lucidum* was popular as a cancer chemotherapy agent in ancient China (Barh *et al.*, 2019).

18. Composition of *Ganoderma lucidium*

Mushrooms in general tend to be 90% water or so, which makes a basic mushroom 'extract' dehydrated mushroom powder (and thus 1g extract, if unspecified, may be about as potent as 10g of the mushroom). Beyond that, they tend to be a good source of protein (10-40% of the non-water weight) carbohydrates (3-28%), fiber (3-32%) and then trace Essential Vitamins or Minerals (Barh*et al*, 2019). Ganoderma is on the high end for fiber, low end for

carbohydrate, moderate to high end for protein and has a relatively low ash (mineral) content. Beyond the basics, Ganoderma Lucidum possesses unique bioactive molecules including:

A variety of Bioactive polysaccharides (Gao *et al*., 2004) that tend to be the components that interact with the immune system (Zhi-bin and Zhang, 2004) and are subdivided into β-1,3-glucans and polysaccharide peptides like peptidoglycan.

Water-soluble polysaccharide peptides, or carbs with amino acids in the structure. They include GLPS; *Ganoderma lucidum* polysaccharide peptide (GLPP) (Hu, *et al*. 2002), GLPG; *Ganoderma lucidum*proteoglycan , GLIS; *Ganoderma lucidum* immunomodulating substance (Jamal *et al*., 2009), PGY; water solube gycopeptide, F3,β-1,3-Glucans (subset of polysaccharides) sometimes called 'Curdlan' (Gao*et al*., 2004) and some other Glucan molecules

Over 120 triterpenoid compounds (Wang, *et al*., 1997, Fatmawati, Shimizu and Kondo, 2011) which can be separated into those with a carboxylic side chain (Ganoderma Acids) and those without (Ganoderma alcohols). Some are referred to as lucidenic acids. (Weng, *et al*., 2007). It has anti-inflammatory, anti-tumorigenic and hypolipidemia properties.

Nucleotide bases (thymine, uridine, inosine, guanosine, adenosine) the sum of all ranging from 303-1217mcg/g (in the mushroom cap) and 22-334mcg/g in the stem.

Some bioactive proteins, such as LZ-8 (Lingzhi-8) (van der *et al.*, 2003) and Ganodermin (Wang *et al*., 1997) a 114kDa hexameric lectin, a glycoprotein with 9.3% sugar. A reversible and highly specific competitive alpha-glucosidase inhibitor known as SKG-3 with an IC50 value of 4.6mcg/mL, Ergostane sterols (Ma, *et al.,* 2002) and ergosterol, known as pro-vitamin D2 (Liu, *et al*., 2011), C19 fatty acids (nonadecenoic acid and cis-9-nonadecenoic acid) (Gao, *et al*., 2012) including Riboflavin, Vitamin C, Copper and Zinc.

Selenium at up to 72mcg/g dry weight (best estimate of wet weight is 7.2ug/g) and can biotransform selenium into selenium-containing proteins. Germanium (the ion, not to be confused with Geranium) at up to 489mcg/g. (Chiu, *et al*., 2000) and the basic analysis of log-cultivated fruit bodies of G. lucidum revealed phosphorus, silica, sulfur, potassium, calcium, and magnesium to be their main mineral components. Iron, sodium, zinc, copper, manganese, and strontium were also detected in lower amounts, as were the heavy metals lead, cadmium, and mercury (Chen *et al.*, 1995).

There is also a large Chitin content in the *Ganoderma lucidum* mushroom, which is indigestible (and for the most part, not bioactive) and makes the mushroom tough to chew. The mushroom is hazel/red in color, which is due to the polysaccharide content.

19. Therapeutic Application of *Ganoderma lucidium*

Ganoderma lucidium has been used for thousands of years as a health promotion and treatment strategy and it has been reported to have a number of pharmacological effects including immune-modulating, anti-inflammatory, analgesic, chemo preventive, anti- tumor, anti- oxidative, anti-viral and bacterial infection, anti-aging, anti-ulcer properties and it's also been recognized as an alternative adjuvant in treatment of leukemia, carcinoma hepatitis, and diabetes (Wasser *et al*., 2005).

20. Anti-oxidant effects

Consumption of anti-oxidant plants may help prevent cancer and other chronic diseases (Benzie *et al.*, 2009) antioxidants protect cellular components from oxidative damage which is likely to decrease risk of mutations and carcinogenesis and also protect immune cells allowing them to maintain immune survelliance and response various components of Ganoderma Lucidium especially polysaccharides and triterpenoids shows antioxidant activities invitro (Choi-Lan *et al.*, 2003) Ooi and Liu (2000) Reported that protein bound polysaccharide (PBP) and polysaccharide peptides were able to mimic endogenous anti-

oxidant superoxide dismutase (SOD) in cancer bearing animals invivo (Ooi *et al.*, 2000)

21. Anti-inflammatory effects

Anti-inflammatory drug make up about half of analgesics, remedying pain by reducing inflammation as opposed to opioids which affect the brain. Joseph et al., showed the anti-inflammatory activity of chloroform extract of *Ganoderma lucidum* in dose dependent carrageenan induced acute and format induced chronic inflammatory models in mice (Soniamol *etal*., 2009). In addition Akihisa et al., also investigated the anti-inflammatory activity of GA-A, -F, -DM and -T-Q in 1-O-tetradecanoylphorbol 13 –acetate- induced inflammation in mice (Akihisa *et al*., 2007).

22. Anticancer effects:

Ganoderma lucidum, an oriental medical mushroom has been used widely in Asian countries for centuries to prevent or treat different diseases including cancer. Dried powder of *Ganoderma lucidum*, which was recommended as a cancer chemotherapy agent, is currently used popularly worldwide in the form of dietary supplements (Jamal Mahajna *et al.*, 2009).*Ganoderma lucidum* extracts were reported to possess cytotoxic activity against various cancer cell lines including leukemia, lymphoma, multiple myeloma (Tomasi S *et al*., 2004) and human breast cancer MCF-7 (Hu H, 2002). The cytotoxic effect of *Ganoderma lucidum* as demonstrated by the studies of Jiang *et al*., and Zhu *et al*., in a concentration dependent manner (Jiang J, *et al*., 2004). This activity of *Ganoderma lucidum* can be attributed directly to specific compounds from experiments employing isolated and purified molecules.

Wang *et al*., (1996) showed that the anti-tumor effect of *Ganoderma lucidum* was mediated by cytokines released from activated T-Lymphocytes and macrophages (Wang *et al*., 1996). *Ganoderma lucidum* could potentiate the production of cytokine including interleukin-1, interleukin-6, tumor necrosis factor, and interferon in which two antitumor cytokines, tumor necrosis factor and interferon, acted synergistically on the inhibition of leukemic-cell growth and markedly induced leukemic - cell apoptosis. The organic Germanium in *Ganoderma lucidum* may also contribute to its anti-tumor activity (Lim *et al*., 1991). W. Tang *et al*., (2006) proposed that GA-T may be a natural potential apoptosis-inducing agent for highly metastatic lung tumor and it may be also applied to treat other tumor cell lines

23. Immuno-modulatory effects

Immunomodulatory properties alone with low cytotoxicity raise the possibility that it could be effective in the cancer patients receiving conventional chemotherapy and/or radiational treatment, to build up immune resistance and decreased toxicity. Numerous experimental and clinical investigations demonstrated that *Ganoderma lucidum* had immunomodulatory activities. A number of reports have demonstrated that *Ganoderma lucidum* polysaccharides stimulated immune function both *in vivo* and *in vitro*. Recent literature has been found that *Ganoderma lucidum* modulate many components of the immune system such as the antigen-presenting cells, NK cells, T and B lymphocytes, macrophages, resulting in the production of cytokines, including interleukins, tumor necrosis factor-α (TNF-α) and interferon (Zhi-bin *et al*., 2004). Chen *et al*., (1995) showed that a crude aqueous extract of *Ganoderma lucidum* probably administered was effective in enhancing the recovery of leukocytes count, splenic blastogenic responses and splenic CD4 and CD8 T cell subsets in mice subjected to γ-irradiation (Chen *et al*., 1995). Choi-Lan-Ha *et al*., (2003) have demonstrated the inhibitory effect of the Chinese herb *Ganoderma lucidum* mycelium on gut immunoglobulin A responses to cholera toxin in mice (Choi-Lan-Ha *et al*., 2003).

24. General Mechanisms of *Ganoderma lucidum*

The immuno-modulating effect of *Ganoderma lucidum* were extensive, including promoting the *function* of antigen-presenting cells, mononuclear phagocytes system, humoral immunity and cellular immunity and cellular immunity and the action site of *Ganoderma lucidum* was speculated to be located in the course of proliferation and differentiation of immune precursor cells to effector cells.

25. Anti-aging effect

Relatively recent research on anti-ageing effect from natural products are of the highest importance for medical stakes (Oncology and immunology) and industrial development (Pharmacy and Cosmetics), it also opens prospects to scientific screening of antioxidizing natural agents among higher fungi (Pourcher *et al*., 2006).

The oxidative damage caused by these free radicals may be related to ageing and diseases, such as atherosclerosis, diabetes, cancer and cirrhosis (Halliwell *et al*., 1984). However, antioxidant supplements or food containing antioxidants may be used to reduce oxidative damage, by not only providing essential vitamins and minerals, but include important chemo-protective agent capable of protecting against some forms of cancer(Ames, 1983). Guesnet *et al*., 2003 stated that GA-B,-C2 and –G have anti-aging effect and can be used as cosmetic agents in various form

26. Specific Mechanisms of *Ganoderma lucidum* on Virus

Using the experiment carried out by Zhang *et al.*,(2014) on Antiviral effects of two Ganoderma lucidum triterpenoids against enterovirus 71 infection to explain it action on virus. They evaluated the antiviral activities of two Ganoderma lucidum triterpenoids (GLTs), Lanosta-7,9(11),24-trien-3-one,15;26-dihydroxy (GLTA) and Ganoderic acid Y (GLTB), against EV71 infection. There results showed that the two natural compounds display significant anti-EV71 activities without cytotoxicity in human rhabdomyosarcoma (RD) cells as evaluated by 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell proliferation assay. The mechanisms by which the two compounds affect EV71 infection were further elucidated by three action modes using Ribavirin, a common antiviral drug, as a positive control. The results suggested that GLTA and GLTB prevent EV71 infection through interacting with the viral particle to block the adsorption of virus to the cells. In addition, the interactions between EV71 virion and the compounds were predicated by computer molecular docking, which illustrated that GLTA and GLTB may bind to the viral capsid protein at a hydrophobic pocket (F site), and thus may block uncoating of EV71. Moreover, they demonstrated that GLTA and GLTB significantly inhibit the replication of the viral RNA (vRNA) of EV71 replication through blocking EV71 uncoating. Thus, GLTA and GLTB may represent two potential therapeutic agents to control and treat EV71 infection.

27. *Persea americana* as an antiviral agent

Persea americana Mill. (*P. americana*) belongs to the family Lauraceae, which is known as (Avocado) and widely grows in tropical and subtropical regions (Collins and Mossman, 2014). The fruit, stem, and leaf of avocado are widely used in ethno-medicine (Brai *et al.*, 2014). Particularly, the avocado fruit contains lots of nutrients such as vitamin E, vitamin B, potassium and monosaturated fatty acids24, which have been reported to exhibit several bioactive properties such as antibacterial (Neeman, 1970), antiviral, antioxidant, anti-atherosclerotic (Akinpelu *et al.*, 2014), hepatoprotective, and other activities (Lu *et al.*, 2012). The bioactive components of avocado contain monoterpenoids, sesquiterpenoids, triterpenoids, favonoids, alkaloids, steroids, carotenoids and long-chain fatty alcohol derivatives (Lu *et al.*, 2012). In a study, carriedout by (Lu *et al.*, 2012) a drug screen of several compounds isolated from the unripe fruit of avocado, including oleic acid (OA), (2R,4R)-1,2,4-trihydroxyheptadec-16-ene (THHE), (2R,4R)-1,2,4-trihydroxyheptadec-16-yne (THHY), avocadenol A, avocadenol C, and avocadoin, and found that THHY exhibited anti-DENV activity without cytotoxicity. We next characterized that THHY inhibits DENV infection through induction of NF-κB-mediated antiviral IFN responses. Finally, we assessed the potential of THHY as a dietary supplement used for prevention of lethal DENV replication using a DENV-infected ICR suckling mouse model (Yu-Hsuan *et al.*, 2019).

28. Phytochemical of Avocado

Phytochemicals are important chemicals found virtually in plants at different parts of the plants in different concentrations. The phytochemical

component presence in Avocado (*Persea* americana) includes saponins which is present in the fruit and seed and some of the general characteristics of this saponins include formation of foams in aqueous solution, haemolytic activity, cholesterol binding properties, e.t.c. Saponins were highest in P. americana seed while the fruit produced the least. Tannins which are another phytochemical is noted for astringency and bitter taste, hasten the healing of wounds and inflamed mucus membrane (Okwu and Okwu, 2004). The low content of tannins in P. Americana leaf and the fruit may be responsible for their free astringency and bitter taste. The flavonoids are potent water-soluble super antioxidants and free radical scavengers. They prevent oxidative cell damage, have strong anticancer activity and protect against all stages of carcinogenesis (Arukwe *et al.*, 2012). Flavonoids in intestinal tract lower the risk of heart disease, inflammation and represent the most common and widely distributed groups of plant phenolic compounds. Flavonoids in leaves and fruits of P.americana are high and could be behind anti-inflammatory, anti-cancer and anti-hypertensive property of the plant and its parts as earlier reported by (Anaka *et al.*, 2009; Imafidon and Amaechina, 2010). Alkaloids are important therapeutically significantly plant secondary metabolites and isolated pure form of alkaloids and their synthetic derivatives are used as basic medicinal agents for their analgesic and bactericidal effects. Phenols have been extensively research as disease preventives and is detected as one of the phytochemicals present in P. americana which further indicate its ability to act as anti-inflammatory, anticlotting, anti-oxidants, immune enhancers, etc. The knowledge of cyanogenic glycosides is important due to their hydrogen cyanic acid (HCN) poison in the body (Onwuka, 2005), but should not pose a problem, since the frequently used parts (leaf and fruit) in phytomedicine are free of this toxic compound. For many years now, it has been known that plant steroids are antioxidants in vitro, and have link with reproduction in humans (Imafidon and Amaechina, 2010).

Their moisture contents are relatively low and could imply long shelf life and the importance of this moisture content in the body of organisms cannot be overstated because they acts as a dissolving medium for substrates, transport materials; regulate temperature, etc (Arukwe et al., 2012). The fruit of P. Americana contain high fat than the seed and the leaves and this give an indication that it could be an oil fruits. Meanwhile, fats have many function in the aside the insulation and conversion of body temperature in an organism in which their fatty acid components such as lauric acid, etc, have been reported to improve their health (Arukwe et al., 2012).

29. Specific mode of action on virus

Using the experiment of Yu-Hsuan *et al*., (2019), on Avocado (*Persea americana*) fruit extract (2R,4R)-1,2,4- trihydroxyheptadec-16-yne inhibits dengue virus (DENV) replication via upregulation of NF-κB–dependent induction of antiviral interferon responses to explain the effect of avocado on virus

30. Avocado extract THHY exhibits anti-DENV activity

Based on the primary anti-DENV screening of several constituents extracted from avocado using a cell-based DENV infectious system, they identified a component (2R,4R)-1,2,4-trihydroxyheptadec-16-yne named THHY, with significant anti-DENV activity. To further confirm the anti-DENV activity of THHY, DENV-infected Huh-7 was incubated with THHY at doses of 0, 1, 5, 10, and 20 μM. Te RNA and protein were harvested to analyze DENV RNA and protein levels at day 3 post-infection, respectively. THHY significantly suppressed DENV-2 RNA and protein synthesis, with EC50 values of 10.98±1.9 μM. As expected, the THHY also inhibited the DENV-2 protein synthesis when compared to the non-THHY treated DENV-infected cells, in which the ribavirin was served as a positive control. In the meantime, the results of the MTS assay indicated no significant cytotoxicity at the effective concentration. Additionally, they further determined the anti-DENV activity of THHY on DENV-1, -2, -3 and -4 (EC50 values of 14.61±2.4, 10.98±1.9, 12.87±1.7 and 14.61±2.1μM). Moreover, they performed a time-dependent antiviral activity assay in Huh-7 cells. Te DENV-infected cells were treated with 20 μM of THHY for diferent period of

time. Following 1, 2, and 3 days post-infection, cell lysates were harvested to analyze DENV protein levels by western blotting. Te data indicated that THHY inhibited DENV replication in a time-dependent manner

31. THHY inhibits DENV replication by NF-κB-mediated IFN production.

Activation of the nuclear factor-κB (NF-κB) signal pathway is considered as a critical factor for stimulating type I IFN responses against pathogen infection (Zhu *et al.,* 2014). Recent research demonstrated that induction of NF-κB- mediated antiviral IFN-α responses could efciently suppress DENV-2 replication13. To characterize how THHY inhibits DENV-2 replication, firstly, they analyzed whether THHY treatment could induce NF-κB activity in the presence of DENV. Huh-7 cells were infected by DENV-2 and then incubated with THHY. Te total cell lysates were harvested at 0.5, 1, 3, and 6h afer treatment, and the phosphorylation status of NF-κB and its upstream regulators including IκBα and IKKα/β were examined by western blotting. THHY treatment resulted in the accumulation of phospho-IKKα/β and phospho-NF-κB levels in a time-dependent manner. In addition, they performed NF-κB promoter-based reporter assay to identify whether NF-κB transcriptional activity was induced by THHY and the THHY dose-dependently induced NF-κB promoter activity upon DENV infection. To further confirm the role of NF-κB on anti-DENV activity of THHY, NF-κB specifc inhibitor, CAPE, was employed to inhibit NF-κB activity in the presence of DENV infection. THHY efectively reduced DENV protein replication (lanes 1 and 2), and the CAPE treatment attenuated the anti-DENV efect of THHY (lanes 2 and 3). They futher examined whether THHY treatment could up-regulate IFN-α levels upon DENV infection. DENV-2-infected Huh-7 cells were incubated with THHY at indicated concentration. The cellular RNA was collected to analyze mRNA levels of FN-α-2 and IFN-α-17 at day 3 post-infection. The results showed that THHY induced both IFN-α RNA level in DENV-2-infected cells. Furthermore, they simultaneously measured the secretory protein level of IFN-α in the supernatant by ELISA. As expected, IFN-α secretion was increased by THHY treatment. Collectively, these results revealed that THHY inhibits DENV replication via up-regulation of NF-κB-mediated antiviral IFN-α expression.

32. Conclusion

Medicinal plants are of great importance in medicine as their role has proven to be of great therapeutic importance. The current review has cited relevant studies that have proven the efficacy of these selected plants (Tumeric, Bitter Kola, *Mimosa pudica*, *Ganoderma lucidium* and *Persea americana*) in the treatment of viral diseases based on their active phytochemical components. Besides, their mode of action such as the production of antioxidants are of great significance as anti-viral agents; these would include the inherent possession (in these plants) of superoxide dismutase, glutathione, catalase and anti-lipid peroxidation activity. In the same vein, the mode of action taking place at the cell cycle is an inevitable tool in the mechanism of action of these antiviral plants. Thus, the tumor/viral suppressor gene P53 is phosphorylated at the G-phase level to bring about P-21 which inhibits the progression of the viral disease at G/S phase road block.

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