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Review on the secondary metabolites, biological properties, and ethnomedicinal uses of the component species of the buheri wa afya formula used to treat COVID-19 in Tanzania

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A R T I C L E I N F O

Keywords:
Buheri wa Afya
Adansonia digitata
Securidaca longipedunculata
Syzygium cumini
Zanthoxylum chalybeum
Ganoderma tsugae

A B S T R A C T

Background: It has proven difficult to treat viral infections like SARS-CoV, MERS-CoV, and SARS-CoV-2 that cause severe respiratory disorders with the currently available medications. Alternative strategies for combating viral infections are required to adequately treat infectious diseases like COVID-19. The most potent of them all may be plant-based products or herbal remedies. Following the advent of the COVID-19 epidemic, a number of alternative medicine practitioners in Tanzania developed herbal medicine formulations, claiming that they were effective in treating COVID-19 patients. One among the formulations is Buheri wa Afya, meaning "good health". The rationale for choosing Buheri wa Afya over the other formulations was justified by its efficacy in treating COVID-19 patients at different stages of the illness.
Purpose: This review aimed to collect information on the chemical composition, biological properties, and ethnomedicinal uses of the constituents of Buheri wa Afya formula, a plant-fungi complex formula made of *Adansonia digitata* L., *Ficus sur* Forssk, *Securidaca longipedunculata* Fresen, *Syzygium cumini* (L.) Skeels, and *Zanthoxylum chalybeum* Engl., and a fungus, *Ganoderma tsugae* Murrill, that was and is still used for the treatment of COVID-19 in Tanzania.
Methods: All information regarding ethnomedical applications, chemical compositions, and biological properties related to the constituents of the herbal formula was collected from PubMed, Research4Life, Google Scholar, Science Direct, Web of Science, Wiley Online Library, Springer, Research Gate link, and published books.
Results: The search, which mostly focused on COVID-19 and other viral infectious diseases produced a total of 183 publications, with publication dates ranging from 1984 to 2023. Most of the articles originated from African and Asian (specifically China and India) countries. A total of 16 articles spanning between 1984 through 1999 reporting on a variety of topics, such as isolation of compounds and biological testing were collected. During that time, *Ganoderma* species had the highest number of reported occurrences. In contrast to the 25 papers collected between 2000 and 2009, 78 articles covering the years 2010 through 2019 were collected. These 103 articles reported studies on ethnomedicinal uses, pharmacological properties, and chemical compositions of the plants and mushrooms under review. During the 2020–2023 period, a total 67 different articles were gathered, the major focus being the fight against COVID-19 and other viral infectious diseases. Twelve of them reported the ethnomedical applications of the investigated plant and mushroom species in the Buheri wa Afya formula in the management and treatment of COVID-19 and associated symptoms. The majority of articles reported the presence of a variety of biologically active compounds, including vitamins, flavonoids, phenols, coumarins, alkaloids, terpenoids, macronutrients, and micronutrients. According to the studies, the compounds have been reported to exhibit anti-inflammatory, immunomodulatory, antiviral, antioxidant, antimalarial and many other biological properties. The combination of the observed biological properties of the plant and mushroom species in the Buheri wa Afya formula may be responsible for its effectiveness in the treatment of COVID-19 in Tanzania.

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Conclusions: The literature has highlighted the indispensable importance of using bBuheri wa Afya as an effective alternative therapy in the management of viral infectious diseases like COVID-19. Various studies reviewed in this study have revealed the potentials of the constituents of Buheri wa Afya in fighting against COVID-19 and other viral infections. Thus, Buheri wa Afya formula with the intrinsic antioxidant, anti-inflammatory, antiviral and immunomodulating properties of its constituents justifies the observed effectiveness of the formula in protection, alleviation of symptoms, and cure of COVID-19 in Tanzania.

Introduction

In Africa and other developing countries about 80 % of the population still depend on medicinal plants in the fight against various ailments. The reliance on ethnomedicine is not only due to the high cost of conventional medicine and inaccessibility to health facilities but also are culturally valued and accepted by most communities (Abdullahi, 2011; Ekor, 2014; Mahomoodally, 2013; Oyebode et al., 2016; WHO, 2004).

Currently, the use of medicinal plants is increasing due to some pathogens are becoming resistant to available synthetic drugs, drug shortages due to population growth and most importantly, ease of availability, affordability, accessibility and promising effectiveness of plants (Ekor, 2014; Mahomoodally, 2013; Marshalls, 1998). Furthermore, the emergence of infectious and pandemic diseases, such as the COVID-19 pandemic in December 2019, has also necessitated the increased reliance on plants or plant-based products as alternatives to fight against the pandemic (Ali et al., 2021). Poor immune regulation and lung fibrosis, which are the primary contributors to SARS-CoV-2 pathogenesis, are the main causes of the poor outcomes in COVID-19 patients. Thus, any herbal remedy with immunomodulatory, antiviral, anti-inflammatory, or antioxidant properties may have the potential to be used as a preventive measure or a therapeutic agent for the treatment of COVID-19 infections (Anand et al., 2021; Khan et al., 2021; Lyu et al., 2021; Nugraha et al., 2020; Ojo et al., 2020; Tran et al., 2022; Zhang and Liu, 2020). Thus, it has been demonstrated that plants are possible promising sources of those natural bioactive substances that can prevent or treat viral illnesses and infections (Alhazmi et al., 2021; Ali et al., 2021; Bafandeh et al., 2023; Khadka et al., 2021; Lyu et al., 2021; Trivedi et al., 2022). The consumption of these herbal medicines with varieties of biological activities, such as antimicrobial, antiviral, anti-inflammatory and immunostimulatory activities, can help to treat infectious diseases, and several other immunologic and inflammatory illnesses including cancer, rheumatoid arthritis, plaque psoriasis, and chronic inflammatory bowel disease (Alhazmi et al., 2021; Ali et al., 2021; Bafandeh et al., 2023; Khadka et al., 2021; Kocaadam and Şanlier, 2017; Lyu et al., 2021; Trivedi et al., 2022). Plant products have been shown to possess potential immunomodulation effects in incidences of acute respiratory infections, such as SARS-CoV, MERS-CoV and SARS-CoV-2 (Alhazmi et al., 2021).

In literature, there are reports of the use of plants, fungi, and their derived products in the management of COVID-19 and other viral diseases, where indigenous knowledge of the species is useful for fighting against the pandemic in Africa and Asia. Studies carried out in several African nations have confirmed that plants and fungi are abundant sources of biologically active substances that can enable an effective fight against the deadly COVID-19 disease (Akindele et al., 2020; Attah et al., 2021; Nkeck et al., 2020; Orisakwe et al., 2020).

Traditional medicine is widely used in Tanzania, and it is a thriving industry in both rural and urban regions (Posthouwer et al., 2016). The use of plants, mushrooms and their chemical constituents as alternatives to pharmaceutical drugs is supported by a number of factors, including ease accessibility, low cost, promising efficacy, and lack of negative side effects.

Following the World Health Organization's (WHO) declaration of COVID-19 as a pandemic in March 2020, various herbal medicines, including buheri wa afya, were developed to treat COVID-19 and other viral diseases in Tanzania. Different plants and mushroom species were used to prepare these medicinal herb formulations, which are presently being used to treat COVID-19. Most of these species have historically been used to treat a number of diseases. For example, inhalation of steam produced by boiling concoctions of Psidium guajava L., Mangifera indica L., Cymbopogon citratus DC. ex Nees, Zingiber officinale Roscoe, Ocimum americanum L., and Azadirachta indica A. Juss. in an earthen pot (locally known as nyungu) was one of the first methods used in Tanzania to combat COVID-19. The procedure, which entails completely enclosing the patient undergoing treatment for 10–15 min, was considered to effective in combating COVID-19 because the steam inhalation clears the respiratory system. In some instances, a blend of cayenne peppers, garlic, lemon, ginger, black pepper, and red onions was prepared for use as a COVID-19 therapy or immune booster (Kombe, 2020; Mshana et al., 2021; Mujinja and Saronga, 2021).

Methodology adopted in this study

All information regarding ethnomedicinal applications, chemical compositions, and biological properties related to the five medicinal plants and the mushroom species was collected from different scientific databases, including PubMed, Research4Life, Google Scholar, Science Direct, Web of Science, Wiley Online Library, Springer, Research Gate link, and published books. Personal communications, unreleased data, and irrelevant material are not included in this review.

Buheri wa Afya (Good Health) is a complex herbal formula used in Tanzania for treating communicable and non-communicable diseases including COVID-19. The formulation is made up of five plant species, *Adansonia digitata* L., *Ficus sur* Forssk, *Securidaca longipedunculata* Fresen., *Syzygium cumini* L. and *Zanthoxylum chalybeum* Engl. and a mushroom species *Ganoderma tsugae* Murrill. The formulation is a commercialized product which is in powder form made by The Nelson Mandela African Institute for Science and Technology in collaboration with TANHELSO, a private company under APPP (Academic-Public-Private Partnership) arrangement. The formula can be dispensed or prescribed in different forms depending on the COVID-19 observed symptoms, development stage, or diagnosed associated diseases. Thus, in addition to a drink or tea, the formula can also be packed in different forms such as capsules, tea bags, tablets, and syrup.

Plant species in buheri wa afya formula

This section provides a review of the information available on the five plant species *A. digitata, F. sur, S. longipedunculata, S. cumini*, and *Z. chalybeum*, that make up the Buheri wa Afya herbal formula.

A. digitata

A. digitata often known as the African baobab tree or Mbuyu in Swahili and a member of the Malvaceae family, is the most common species of the genus *Adansonia* and is indigenous to Africa and the southern Arabian Peninsula (Kew Science, 2023; Rahul et al., 2015). Seeds, leaves, roots, flowers, fruit pulp, and bark of baobab are edible. The different parts of the baobab plant have been extensively used in ethnomedicine since ancient times for the treatment of various illnesses, including diarrhea, malaria and microbial infections as shown in Table 1 (De Caluwé et al., 2010; Kamatou et al., 2011). The plant is also reported as an antipyretic or febrifuge, anti-dysenteric, diaphoretic, immunostimulant, anti-inflammatory, analgesic and probiotic remedy.

Table 1
Ethnomedicinal uses of the plant species in Buheri wa Afya formula used in the management of COVID-19 in Tanzania.

Plant Name	Plant parts	Ethnomedicinal uses	References
A. digitata L. (Malvaceae) Swahili: Mbuyu	Seeds, leaves, roots, flowers, fruit pulp and bark	Treatment of diarrhea, malaria, microbial infections, tuberculosis, fever, anemia, dysentery, toothache, as an immune stimulant, stimulation of milk production in breastfeeding women, flavouring agent, or roasted and eaten as snacks and treatment of COVID-19.	(Braca et al., 2018; De Caluwé et al., 2010; Eltahir and Elsayed, 2019; Kamatou et al., 2011; Malabadi et al., 2021)
F. sur Forssk. *(Moraceae); Mkuyu/Mvumo*	Leaves, stem and root barks	Treatment of diabetes, stomach ache, piles, skin diseases, inflammation, cancer, malaria and management of viral induced diseases such as COVID-19.	(Lumbile and Mogotsi, 2008; Nawaz et al., 2020; Raimi et al., 2022; Ramde-Tiendrebeogo et al., 2012)
S. longipedunculata Fresen. (Polygalaceae); Swahili: Muteya or mzingi	All parts	Treatment of sexually transmitted infections, hernias, coughs, fever, ascariasis, constipation, headaches, rheumatism, stomach ache, malaria, tuberculosis, pain, epilepsy, pneumonia, skin infections, typhoid, inflammation, viral infections, dysentery, snake bites, used as an aphrodisiac for men, pesticide against beetles.	(Meli Lannang et al., 2006; Mongalo et al., 2015; Nakaziba et al., 2021; Stevenson et al., 2009; Suleiman Abubakar et al., 2019)
S. cumini L. (Myrtaceae); Swahili: Mzambarau	Leaf, fruit, bark and seed	Treatment of cough, bronchitis, diabetes and related complications, biliousness, dysentery, inflammation, ulcers, ringworm, cancer, blisters in mouth, diarrhea, digestive complaints, piles, pimples and stomach ache.	(Aqil et al., 2014; Ayyanar and Subash-Babu, 2012; Kumar et al., 2009a; Mohamed et al., 2013; Peixoto and Freitas, 2013; Siani et al., 2013)
Z. chalybeum Engl. (Rutaceae)*; Swahili: Mjafari*	Leaves, stem and root barks	Treatment of malaria, sickle cell disease, measles, skin infections, fever, headaches, chest pain, digestive illnesses (e.g. ulcers), diabetes, toothache and coughs, used in arrow poison.	(Agyare et al., 2013; Evariste, 2020; Jacqueline et al., 2018; Orwa et al., 2009; Tabuti, 2011)

Furthermore, the fruit pulp is used to treat diarrhea of children and to stimulate the milk production in breastfeeding women and for the treatment of COVID-19 (Braca et al., 2018; Malabadi et al., 2021). Due to its high protein, zinc, and vitamin C content, the baobab fruit pulp acts as an immunogenic agent and promotes the development of immunity to COVID-19. According to reports, the baobab fruit pulp was used in India as an immunity booster to suppress the virus and helped many COVID-19 patients by slowing the virus' spread during the Delta variant (B.1.617.2) and Delta Plus (AY.1) coronavirus outbreaks (Malabadi et al., 2021). Additionally, the leaves, bark and seeds are used for the treatment of malaria, tuberculosis, fever, microbial infections, diarrhea, anemia, dysentery, toothache and as immune stimulant (Table 1) (Eltahir and Elsayed, 2019). The leaves have also been used in the preparation of soup, whereas the seeds are used as a thickening agent in soups, and they can be fermented and used as a flavoring agent or roasted and eaten as snacks (Donatien, 2011).

A. digitata showed to have antioxidant and anti-inflammatory (Tembo et al., 2021), hepatoprotective (Hanafy et al., 2016), cardioprotective (Ghoneim et al., 2016), antidiabetic (Irondi et al., 2017), and antitumor activities (Elsaid, 2013). The methanol extract was reported to exhibit antioxidant and anti-inflammatory effects (Irondi et al., 2017), whereas the leaf extracts showed anti-inflammatory effects in LPS-stimulated RAW264.7, by reducing iNOS and NF-κB expression, with possible involvement of other pathways (Table 2) (Ayele et al., 2013; Cuviello et al., 2015).

Phytochemical studies of *A. digitata* have led to the isolation of flavonoids, catechins, procyanidins (A2, B2, B5, and C1), tirilosides, and other substances like citric acid, feruloylquinic acid gallic, chlorogenic, caffeic, and ellagic acids (Braca et al., 2018; Tsetegho Sokeng et al., 2019). The reported flavonoids are quercetin, kaempferol, luteolin, and their glycosides (Braca et al., 2018; Tsetegho Sokeng et al., 2019). Fig. 1 and Table 3 present some of the important phytochemicals reported from *A. digitata*.

Analysis of the essential oils from the stem bark and leaves of *A. digitata* revealed the presence of different types of constituents, such as caryophyllene, humulene, tetramethyl-2-hexadecen-1-ol, 8-dimethyl-2-(1-methylethenyl), heptacosane, cyclopentane, heptadecane, and tetracosane. The essential oils from leaf and stem bark exhibited significant antimicrobial activity and toxicity against brine shrimps (Kayode et al., 2018).

Ficus sur

F. sur (Swahili: Mkuyu, mkuju, mwangajo), family Moraceae, is a medium-sized tree widely distributed throughout tropical Africa and Yemen (Fern, 2014, Lumbile and Mogotsi, 2008), which showed to be effective in the treatment of diabetes, stomachache, piles, skin diseases, inflammation, cancer and management of viral-induced diseases such as COVID-19 (Esievo et al., 2018; Nawaz et al., 2020; Raimi et al., 2022; Ramde-Tiendrebeogo et al., 2012). The ethnomedicinal uses of the different parts of *F. sur* are presented in Table 1.

The leaf, stem and root bark extracts have been reported to possess *in vitro* antibacterial, anti-inflammatory, fibrinolytic and antioxidant activities (Fern, 2014; Mikailu et al., 2022; Ramde-Tiendrebeogo et al., 2012), whilst the methanol extracts of the leaves, stem and root barks

Table 2
Phamacological properties of the plant species in Buheri wa Afya formula used in the management of COVID-19 in Tanzania.

Plant Name	Parts of Plant	Pharmacological properties	References
A. digitata L. (Malvaceae) Swahili: Mbuyu	All parts	Anti-oxidant, anti-inflammatory, hepatoprotective effect, cardioprotective, antidiabetic, and antitumor activities.	(Ayele et al., 2013; Cuviello et al., 2015; Elsaid, 2013; Ghoneim et al., 2016; Hanafy et al., 2016; Irondi et al., 2017; Malabadi et al., 2021; Tembo et al., 2021)
Ficus sur Forssk. *(Moraceae);* Swahili: *Mkuyu/ Mvumo*	Leaves, stem and root barks	Antibacterial, antidiabetic, antiviral towards HHV-1, antioxidant, anti-inflammatory, antiulcer, anticonvulsant, antimalarial activities and spasmolytic effects.	(Nawaz et al., 2020; Ngoh Misse Mouelle et al., 2022; Ogunlaja et al., 2022; Ramde-Tiendrebeogo et al., 2012; Saloufou et al., 2018; Sieniawska et al., 2022)
S. longipedunculata Fresen. (Polygalaceae); Swahili: Muteya or mzingi	All parts	Antimicrobial, antioxidant, antiparasitic, anti-diabetic, anti-inflammatory, antimalarial, insecticidal, enzyme inhibition, molluscicidal, pesticidal, and anticonvulsant activities.	(Dibwe et al., 2012; Meli Lannang et al., 2006; Mongalo et al., 2015; Namadina et al., 2020; Stevenson et al., 2009; Suleiman Abubakar et al., 2019)
S. cumini L. (Myrtaceae); Swahili: Mzambarau	Leaf, fruit, bark, flowers, and seed	Antidiabetic, hypolipidemic, cardioprotective, antidiarrheal, antiallergic, antifertility, antipyretic, anti-clastogenic, anti-inflammatory, antiviral, antimicrobial, antidermatophytic, anti-HIV, antiarthritic, anti COVID-19.	(Aini et al., 2022; Aqil et al., 2014; Ayyanar and Subash-Babu, 2012; Kumar et al., 2009a; Peixoto and Freitas, 2013; Renjana et al., 2021)
Z. chalybeum Engl. (Rutaceae)*;* Swahili: *Mjafari*	Leaves, stem and root barks	Antibacterial, antimalarial and antiviral activities, trypanocidal activity, antiviral activity against measles virus and anti COVID-19.	(Adia et al., 2016; Agyare et al., 2013; Evariste, 2020; Freiburghaus et al., 1996; Freiburghaus et al., 1997; Gessler et al., 1995; Jacqueline et al., 2018; Kiraithe et al., 2016; Muema et al., 2021; Muganga et al., 2014; Nakaziba et al., 2021; Nibret et al., 2010; Ocheng et al., 2016; Pierre and Emmanuel, 2013; Rukunga et al., 2009)

are reported to have *in vivo* antimalarial activities (Lumbile and Mogotsi, 2008; Muregi et al., 2003, 2006, 2007). The methanol extract of the stem bark demonstrated substantial *in vitro* antioxidant potentials. Aditionally, the stem bark infusion and methanol extract exhibited anti-neoplastic activity against cervical adenocarcinoma and colon cancer cell lines (Sieniawska et al., 2022), whereas the leaves and fruits methanol extracts have been reported to exhibit antiviral activity against Human Herpesvirus-1 (HHV-1) and antioxidant activity, respectively (Sieniawska et al., 2022). The presence of the antiradical and antibacterial activities of *F. sur* extracts provide scientific support of their traditional use in the treatment of sickle cell disease. In addition, the sap showed antibacterial activity on some pathogenic germs related to sickle cell disease (Ramde-Tiendrebeogo et al., 2012). The aqueous and methanol extracts of the dried leaves have shown *in vivo* anti-ulcer activity and *in vitro* spasmolytic effects (Fern, 2014). Table 2 presents the biological properties of *F. sur*.

Phytochemical studies of the extracts of the different parts of *F. sur* have revealed the presence flavonoids, flavonoid glycosides and other phenolic compounds which have been reported to exhibit antioxidant activity (Ogunlaja et al., 2022; Saloufou et al., 2018). The flavonoid and flavonoid glycosides compositions comprise quercetin-3-*O*-arabino-glucoside, quercetin-*O*-glucoside, kaempferol-*O*-pentoside-hexoside, kaempferol-3-*O*-rhamnosyl galactoside, luteolin, apigenin as well as procyanidin B (Sieniawska et al., 2022). The flavonoids and procyanidin B were also reported from *A. digitata* (Fig. 1) (Braca et al., 2018; Tsetegho Sokeng et al., 2019). Phytochemical investigation of the aerial roots of F. sur, yielded suroside, suramide, alpinumisoflavone, wighteone metabolite, oleanolic acid and epi-ψ-taraxastanolone. Wighteone exhibited a weak cytotoxic activity against the human HepG2 hepatocellular carcinoma cells with an IC_{50} value of 51.9 μM (Ngoh Misse Mouelle et al., 2022; Ogunlaja et al., 2022). The presence of these bioactive compounds with antiviral, immune-modulating properties, macronutrients, and micronutrients in *F. sur* and many other plant species might be the possible reason for their effectiveness in the management of COVID-19 pandemic (Raimi et al., 2022). Fig. 2 and Table 3 show some of the selected phytochemicals isolated from *F. sur* in addition to the flavonoids in Fig. 1.

Studies on the essential oils of the different parts of *F. sur* revealed the presence of *α*-cadinol, *α*-pinene, geranyllinalool, *n*-tetradecane, *α*-humulene and *α*-ionone, *n*-hexadecanoic acid, *α*-pinene, *β*-pinene, *α*-humulene, limonene, and *m*-cymene (Aboaba et al., 2012). The essential oils have been reported to exhibit toxicity in the brine shrimps test which can be linked with antibacterial, pesticidal, cytotoxic, and antitumor properties. According to reports, *n*-hexadecanoic acid contains antioxidant and anticancer (Jayasree Radhakrishnan and Venkatachalam, 2020), pesticidal (Adeyemi et al., 2022), and anti-inflammatory properties (Aparna et al., 2012).

In other studies, the antimicrobial potential of the essential leaf oil of *Ficus capensis* was also investigated using *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Klebsiella* spp., *Proteus spp*., *Pseudomonas* spp., *Salmonella* spp., *Penicillium notatum*, and *Rhizopus stolonifera* with MIC values ranging from 0.08 to 10 mg/ml. The oil is reported to be active against all the microorganisms except *Klebsiella* spp. (Aboaba et al., 2012; Adeyemi et al., 2022; Lawal et al., 2016).

S. longipedunculata

S. longipedunculata, also as violet tree, fiber tree, or Muteya/Mzingi in Swahili, family Polygalaceae, is a native African medicinal plant frequently found in sub-Saharan Africa's Savannah and Sahel settings. The plant is reported to possess a wide range of medicinal, pharmacological, and therapeutic properties and has been used for a variety of purposes in African traditional medicine (Anjarwalla et al., 2015; Mahomoodally, 2013; Maroyi, 2013).

Nearly all parts of S. longipedunculata have been reportedly to be used for the treatment of a variety of illnesses (Table 1), including sexually transmitted infections, hernias, coughs, fevers, ascariasis, constipation, headaches, rheumatism, stomachaches, malaria, tuberculosis, pain, epilepsy, pneumonia, skin infections, typhoid, inflammation, viral infections, dysentery, snake bites, and for the management of the COVID-19 related symptoms (Meli Lannang et al., 2006; Mongalo et al., 2015; Nakaziba et al., 2021). The entire plant is used to wash the mouth and treat infections such as oral candidiasis (Mongalo et al., 2015).

According to studies on the biological properties of the plant's extracts from its various parts, *S. longipedunculata* has been found to

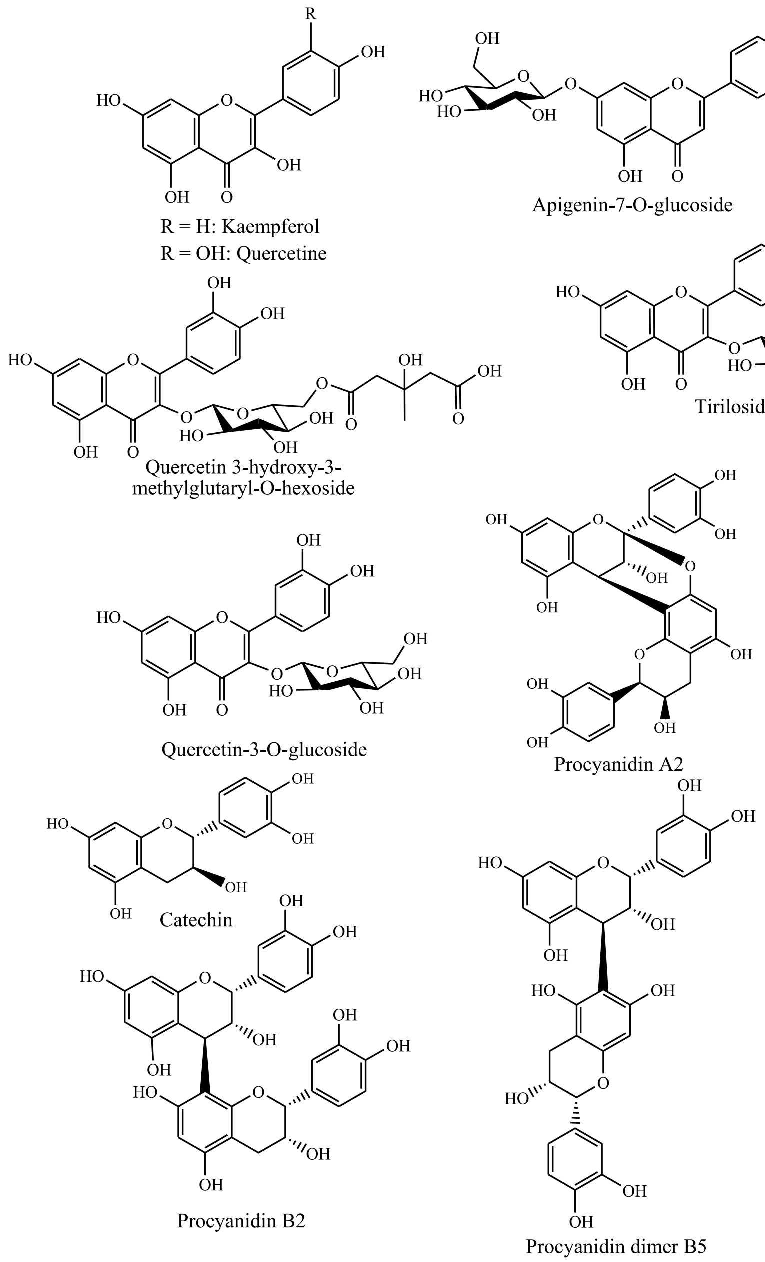

Fig. 1. Some of the selected phytochemical constituents of *Adansonia digitata*.

exhibit antimicrobial, antioxidant, antiparasitic, antidiabetic, anti-inflammatory, antimalarial, insecticidal, molluscicidal, pesticidal, and anticonvulsant activities (Table 2). Furthermore, toxicity studies have shown the extract to be only toxic at relatively high concentrations (Mongalo et al., 2015; Suleiman Abubakar et al., 2019). The powdered dry root bark of *S. longipedunculata* has been reported to be used as pesticide against beetles, *Sitophilus zeamais* and *Callosobruchus maculatus*, in stored grains (Stevenson et al., 2009). Moreover, it is reported to display potent preferential cytotoxicity against the human pancreatic cancer PANC-1 cell line under nutrient-deprived medium (Dibwe et al., 2014a). The leaf and root bark extracts have been reported to exhibit antibacterial and antifungal activities, whereas the stem bark extract was also reported to possess antibacterial activities against clinical isolates of *E. coli, Salmonella typhi, Staphylococcus aureus, Shigella dysenteriae, Pseudomonas aeruginosa* and *Klebsiella pneumonia.* The methanol root bark extracts are reported to exhibit anti-inflammatory activity (Table 2) (Lijalem and Feyissa, 2020; Suleiman Abubakar et al., 2019).

Studies of the essential oils of *S. longipenduculata* revealed the presence of both volatile and non-volatile compounds including *α*-pinene, *β*-pinene, mesitylene, *α*-phellandrene, 8-cineole, p-cymene, nonanal, methyl salicylate, ethyl salicylate, pentadecane, caryophyllene oxide, *α*-cadinol, hexyl salicylate, and a fatty acid, *n*-hexadecanoic acid (Fig. 7) (Adebayo et al., 2007). Among the volatile substances, methyl salicylate, which has been reported to be the major component, it has repellent and toxic properties to *Sitophilus zeamais* adults (Jayasekara et al., 2002, 2005) whereas *n*-hexadecanoic acid is reported to have antioxidant, anticancer, pesticidal, and anti-inflammatory properties (Adeyemi et al., 2022; Aparna et al., 2012; Jayasree Radhakrishnan and Venkatachalam, 2020).

Phytochemical studies of the extracts from various parts of *S. longipedunculata* led to the isolation of xanthones, benzyl benzoates, flavonoids, anthraquinones, alkaloids and triterpene saponins amongst others as shown in Fig. 3 and Table 3 (Dibwe et al., 2012, 2014a, 2014b, 2014c; Meli Lannang et al., 2006; Mongalo et al., 2015; Stevenson et al., 2009; Suleiman Abubakar et al., 2019). The root bark of *S. longipedunculata* yielded a series of twelve highly oxygenated

Table 3
Phytochemical composition of the plant species in Buheri wa Afya formula used in the management of COVID-19 in Tanzania.

Species name	Chemical composition	References
A. digitata L. (Malvaceae) Swahili: Mbuyu	Flavonoids, catechins, procyanidines, tirilosides, citric acid, feruloylquinic acid, catechin, epicatechin, procyanidins, A2, B2, B5 and C1, gallic, chlorogenic, caffeic, and ellagic acids and the essential oils.	(Braca et al., 2018; De Caluwé et al., 2010; Eltahir and Elsayed, 2019; Irondi et al., 2017; Kayode et al., 2018; Tsetegho Sokeng et al., 2019)
F. sur Forssk. *(Moraceae); Mkuyu/Mvumo*	Flavonoids and flavonoidal glycosides, alpinumisoflavone, procyanidin B, alkaloids such as suroside, suramide, lucidine B, phaeophytin, teleocidin B1, terpenoids, oleanolic acid, epi-ψ-taraxastanolone and essential oils components.	(Ngoh Misse Mouelle et al., 2022; Ogunlaja et al., 2022; Saloufou et al., 2018; Sieniawska et al., 2022)
S. longipedunculata Fresen. (Polygalaceae); Swahili: Muteya/ mzingi	Flavonoids, xanthones, benzyl benzoates, anthraquinones, alkaloids (securinine) and triterpene saponins and the essential oils.	(Dibwe et al., 2012, 2014a, 2014b, 2014c; Meli Lannang et al., 2006; Mongalo et al., 2015; Stevenson et al., 2009; Suleiman Abubakar et al., 2019)
S. cumini L. (Myrtaceae); Swahili: Mzambarau	Anthocyanins, diglucosides of delphinidin, petunidin, malvidin, peonidin, and cyanidin, ellagitannins, jambosine, gallic acid, ellagic acid, corilagin and the essential oils.	(Ayyanar and Subash-Babu, 2012; Chhikara et al., 2018; Kumar et al., 2009, 2009; Kumar Bijauliya et al., 2017; Qamar et al., 2022; Sarma et al., 2020; Tak et al., 2022; Uddin et al., 2022)
Z. chalybeum Engl. (Rutaceae)*; Swahili: Mjafari*	Alkaloids such as (+)-magnoflorine, chelerythrine, nitidine (+)-*N*-methylplatydesmine, (-)-oblongine, (-)-usambarine, (-)-*cis-N*-methylcanadine, (+)-tembetarine, jatrorrhizine, palmatine, 4-(isoprenyloxy)-3-methoxy-3,4-deoxymethylenedioxyfagaramide, lignins, coumarins, flavonoids, terpenes and the essential oils.	(Adia et al., 2016; Krohn et al., 2011; Muganga et al., 2014; Okagu et al., 2021; Olila et al., 2001; Omosa et al., 2021; Chisowa et al., 1999)

xanthones, the muchimangins A-L (Dibwe et al., 2012, 2014a, 2014b, 2014c). The compounds were isolated from *S. longipedunculata* collected (Dibwe et al., 2012, 2014a, 2014b, 2014c) in the Democratic Republic of Congo (Dibwe et al., 2012, 2014a, 2014b, 2014c). Among them, muchimangin B is reported to induce an apoptotic-like cell death of human pancreatic cancer PANC-1 cell line (Dibwe et al., 2012).

Further phytochemical investigation of the methanolic extract of *S. longepedunculata* yielded two bisdesmosidic saponins securidacaside A and B (Fig. 3). Securidacaside A, showed deterrence and toxicity toward *C. maculatus* and *S. zeamais* which could be linked with the biological activity of the methanol extract (Stevenson et al., 2009).

S. cumini

S. cumini (known as Jamun in Asia or Mzambarau in Swahili), is an evergreen tropical medicinal plant from the Myrtaceae family. According to reports, the plant has been traditionally used to cure a number of illnesses, including diabetes (Ayyanar and Subash-Babu, 2012; Chagas et al., 2015; Qamar et al., 2022). The plant is also traditionally administered to females who have a history of abortions and used to treat diarrhea. Table 1 summarizes the different ethnomedicinal applications of the plant. According to various reports, the plant's different parts have therapeutic potentials, including hypolipemic, anti-inflammatory, antihyperglycemic, cardioprotective, and antioxidant activities. These properties may be related to the presence of bioactive substances like phenols, flavonoids, and tannins in different plant parts (Aqil et al., 2014; Ayyanar and Subash-Babu, 2012; Chagas et al., 2015; Kumar et al., 2009; Qamar et al., 2022).

Different types of biological activities have been reported from different studies on the biological activities of the fruits of *S. cumini* (Table 2). Activities such as antidiabetic, hypolipidemic, cardioprotective, antidiarrheal, antiallergic, antifertility, antipyretic, anticlastogenic, anti-inflammatory, gastroprotective, antidermatophytic, antimicrobial, antiviral, antianemic, carminative, antioxidant, antineoplastic, radioprotective, anti-HIV, diuretic, anticancer, anorexigenic, antiarthritic, aphrodisiac, antiscorbutic and cytotoxic have been reported for the plant (Aqil et al., 2014; Kumar et al., 2009; Peixoto and Freitas, 2013).

Phytochemical studies of the different parts of the plant have revealed the presence of various primary and secondary metabolites like carbohydrates, proteins, amino acids, alkaloids, flavonoids, phenolic acids, and anthocyanins (Ayyanar and Subash-Babu, 2012; Chhikara et al., 2018; Uddin et al., 2022). The flavonoids include isoquercetin, kaempferol, myricetin, dihydromyricetin and flavonoid glycoside, rutin, whereas the phenolic compounds are gallic, caffeic, and ellagic acids and the anthocyanins glycosides include delphinidin-3,5-O-diglucoside, petunidin-3,5-O-diglucoside, malvidin-3,5-O-diglucoside. According to claims, the seeds contain the glycoside jambolin or antimellin and the alkaloid jambosine, which prevent the diastatic conversion of starch to sugar (Ayyanar and Subash-Babu, 2012; Chhikara et al., 2018; Uddin et al., 2022). In addition, studies have also shown the presence of delphinidin, petunidin, malvidin, peonidin, cyanidin, ellagitannins, jambosine, corilagin and the essential oils as presented in Fig. 4 and Table 3 (Ayyanar and Subash-Babu, 2012; Kumar et al., 2009; Sarma et al., 2020; Tak et al., 2022). The presence of the glycoside jambolin or antimellin and the alkaloid jambosine in the seeds is associated with the prevention of the diastatic conversion of starch to sugar (Ayyanar and Subash-Babu, 2012). Studies have revealed that the presence of phytochemicals, such as betulinic acid, kaempferol, malvidin, myricetin, and quercetin, which interact with ACE2, spike protein, 3CLpro, and PLpro and may have potential anti-COVID-19 properties reported in literature for the plant species (Aini et al., 2022; Renjana et al., 2021).

Analysis of the essential oils from *S. cumini* revealed the presence of different chemical substances, including τ-cadinol and τ-muurolol, globulol, caryophyllene, δ-cadinene and α-pinene (Sarma et al., 2020), β-pinene, 1,3,6-octatriene, delta-3-carene, and limonene as presented in Fig. 7 (Mohamed et al., 2013). The essential oils from *S. cumini*, are reportedly to be biologically active against both stages of *Leishmania amazonensis*, while being safe for mammalian cells (Rodrigues et al., 2015), as well as exhibiting anti-inflammatory (Siani et al., 2013), antioxidant and antibacterial activities (Mohamed et al., 2013).

Z. chalybeum

Z. chalybeum (Rutaceae), also known as Mjafari in Swahili, is a deciduous spiny shrub or tree, of medium to low altitudes very common in Sub-Saharan Africa mostly in Eastern and Southern Africa (Agyare et al., 2013). The plant is popular in ethnomedicinal uses in East Africa, harvested from the wild for local use as tea, medicine, toothbrush and timber (Agyare et al., 2013). Historically, decoctions of Z. chalybeum have been used to treat conditions like malaria, sickle cell anemia, measles, skin infections, fever, headaches, chest pain, digestive disorders (such as ulcers), diabetes, toothache and coughs (Agyare et al., 2013; Jacqueline et al., 2018; Orwa et al., 2009; Tabuti, 2011).

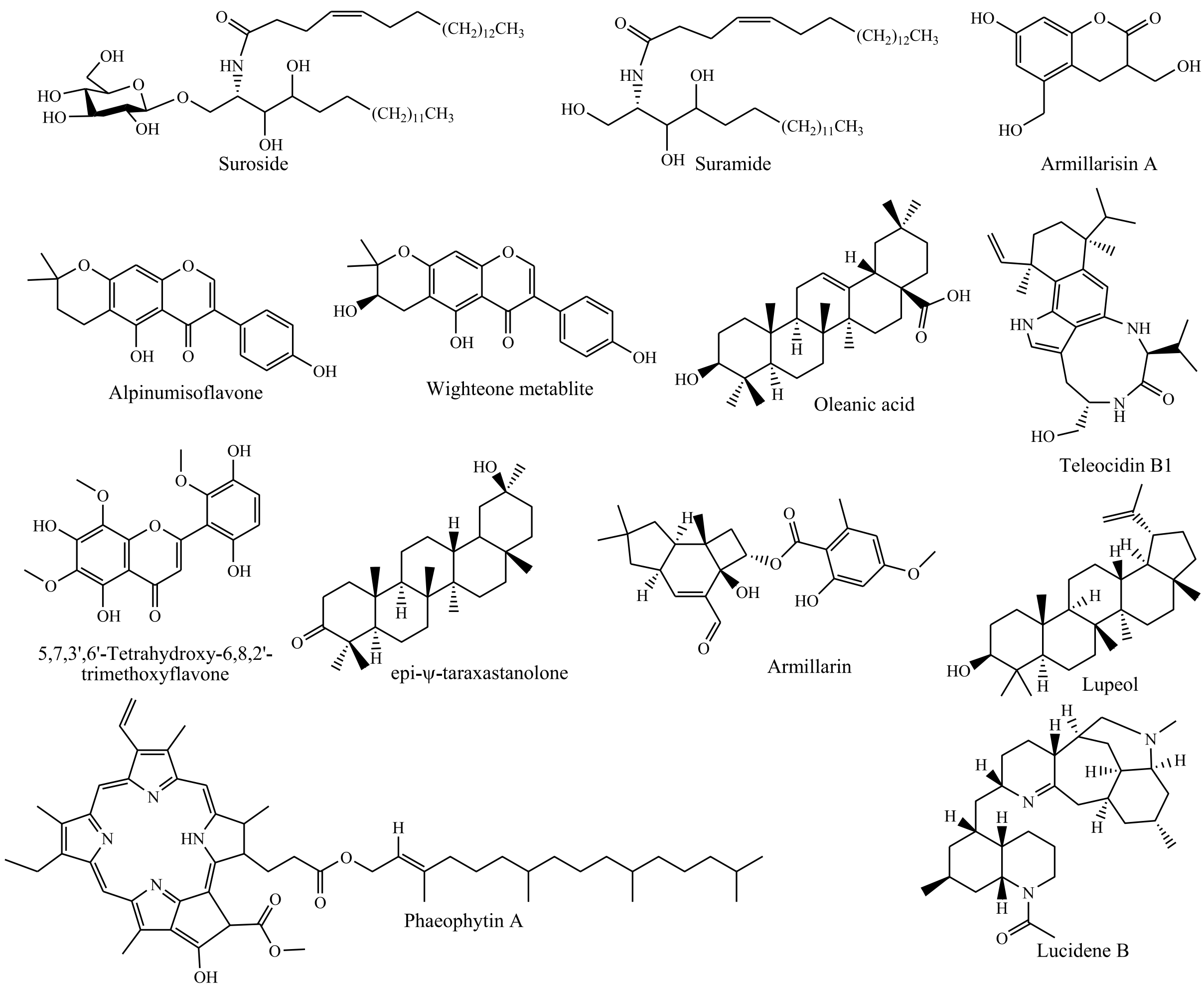

Fig. 2. Phytochemicals isolated from *Ficus sur*.

According to reports, the water extracts are used to cure livestock illnesses, whilst the leaf decoction is utilized to treat intestinal tract infections in cattle (Tabuti, 2011). Furthermore, various studies have revealed that phytochemicals from the *Zanthoxylum* plant species, such as alkaloids and polyphenols, have been shown to have anti-inflammatory, antiviral, antibacterial, and antiplasmodial properties. For example, compounds like, sanguinarine and skimmianine have been reported to exhibit anti-inflammatory and antiviral inhibitory effects, respectively, properties which can be associated with the reported ability in the management of COVID-19 (Evariste, 2020). Table 1 provides an overview of the ethnomedical applications of *Z. chalybeum*.

Research on the biological effects of several extracts from various parts of *Z. chalybeum* have revealed the plant to possess antibacterial, antimalarial, and antiviral activities as depicted in Table 2 (Gessler et al., 1995; Kiraithe et al., 2016; Muema et al., 2021; Ocheng et al., 2016; Pierre and Emmanuel, 2013). According to research on its antimalarial activity conducted in Tanzania and Kenya, the plant showed antimalarial activity (Gessler et al., 1995; Kiraithe et al., 2016; Muema et al., 2021). The results of the two studies provide a basic method for making potential mosquito repellents from *Z. chalybeum* root components (Muema et al., 2021). Previous researches showed that *Z. chalybeum* has antimalarial potency (Adia et al., 2016; Correa-Barbosa et al., 2023; Gessler et al., 1995; Kiraithe et al., 2016; Muema et al., 2021; Muganga et al., 2014; Pierre and Emmanuel, 2013; Rukunga et al., 2009; Stangeland et al., 2010). High activities have been found for the methanol and dichloromethane extracts of root bark (Correa-Barbosa et al., 2023). Studies conducted in Tanzania, Kenya, Uganda and Rwanda, have reported strong activity against *Plasmodium falciparum*, where both root and stem bark extracts were reported to be effective against the multidrug resistant *P. falciparum* stain K1 and a chloroquine resistant strain NF54 (Adia et al., 2016; Gessler et al., 1995; Kiraithe et al., 2016; Muema et al., 2021; Muganga et al., 2014; Pierre and Emmanuel, 2013; Rukunga et al., 2009; Stangeland et al., 2010).

Additionally, strong trypanocidal activity against *Trypanosoma brucei* has also been reported for the plant (Freiburghaus et al., 1996, 1997; Nibret et al., 2010), whereas the aqueous, hexane, and methanol extracts have been reported to exhibit anti-inflammatory activity using the COX-1 assay (Agyare et al., 2013). The ethanol extract of the stem bark exhibited antibacterial activities against *S. typhi, Pseudomonas aeruginosa* and *Staphylococcus aureus* (Pierre and Emmanuel, 2013). The extracts showed some signs of acute toxicity in the brine shrimp lethality tests whereby no signs of toxicity were observed in the mice at a dose of 2000 mg/kg of the crude extracts (Kiraithe et al., 2016).

Essential oils from *Z. chalybeum* exhibited strong cytotoxicity to human gingival fibroblasts and human leukemia HL-60 cells, which could be linked with the high amounts of geranial and neral contents (Ocheng et al., 2016). The essential oils could be used as larvicidal agents to treat human anisakidosis. Furthermore, the essential oils have also been reported to exhibit strong *in vitro* antibacterial activities against *Salmonella thyphi, Streptococcus. agalactia, Staphylococcus aureus and E. coli* and slight antifungal activities against *Aspergillus niger* and *Fusarium oxysporium* (Molla Tigneh and Babu G, 2020). Table 2 gives the summary of the biological activities of Z. chalybeum.

Phytochemical investigations of the various parts of Z. chalybeum lead to the isolation of alkaloids, flavonoids, terpenoids, and lignans and many others (Adia et al., 2016; Krohn et al., 2011; Muganga et al., 2014;

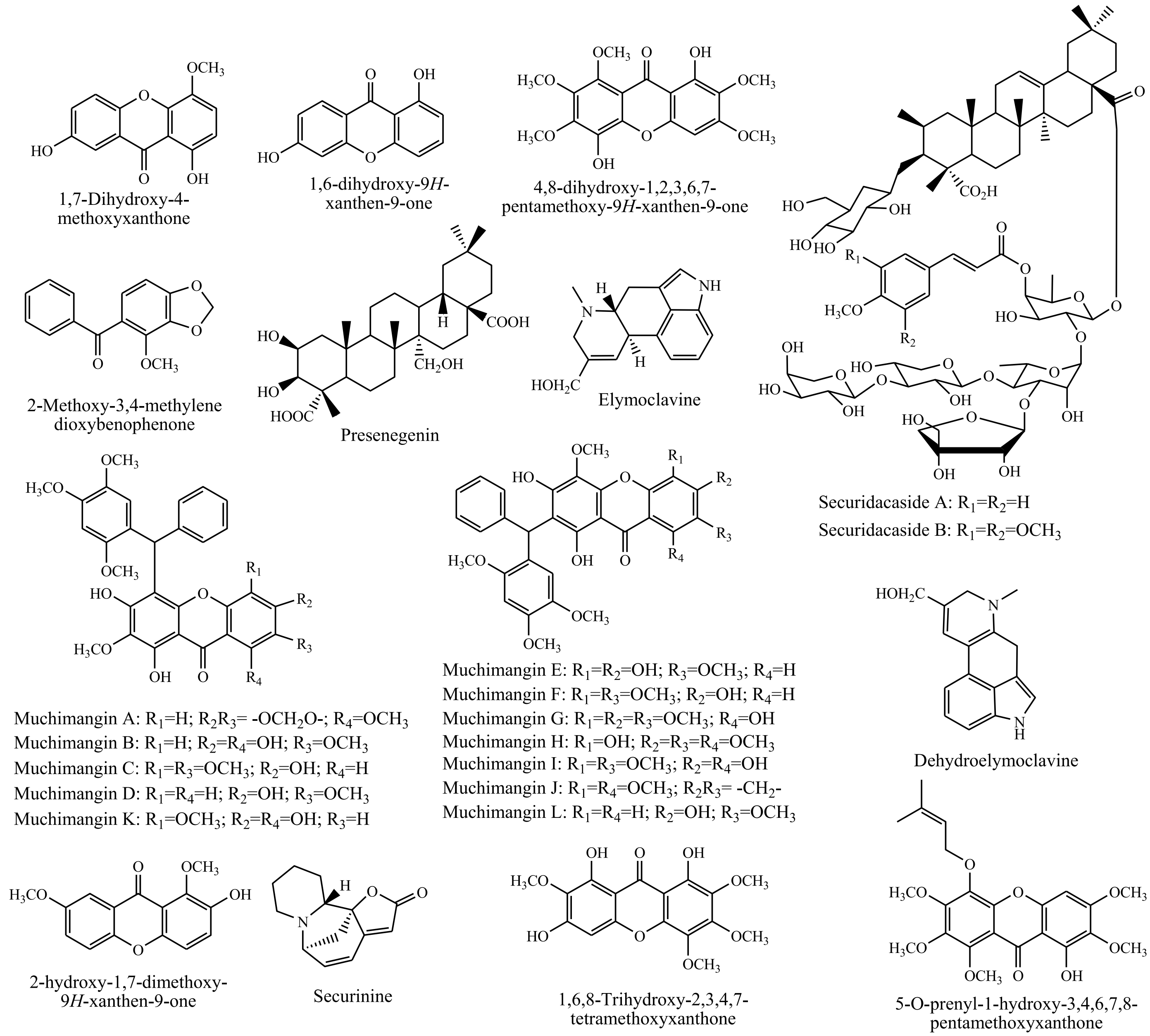

Fig. 3. Selected phytochemicals from *Securidacalongipedunculata*.

Okagu et al., 2021; Olila et al., 2001; Omosa et al., 2021). Thus, studies of the root bark led to the isolation of several alkaloids, (+)-magnoflorine, chelerythrine, nitidine (+)-*N*-methylplatydesmine, (-)-oblongine, (-)-usambarine, (-)-*cis-N*-methylcanadine, (+)-tembetarine, jatrorrhizine and palmatine (Krohn et al., 2011).

The stem bark yielded an alkamide, 4-(isoprenyloxy)-3-methoxy-3,4-deoxymethylenedioxyfagaramide and other alkaloids (Omosa et al., 2021). The seeds yielded an alkaloid, skimianine, which did not have antimicrobial activity (Olila et al., 2001). Fig. 5 and Table 3 give some of the compounds obtained from *Z. chalybeum*.

Fagaramide was reported to exhibit a moderate activity (IC_{50} of 2.85 mg/ml) against the chloroquine-resistant strain than the chloroquine-sensitive (IC_{50} 16.6 mg/ml) strain used in the study (Adia et al., 2016; Muganga et al., 2014), whereas skimmianine is reported to exhibit *in vitro* antiviral activity against measles virus that causes the burning sensation (Anywar et al., 2020, 2022).

Protobeberine alkaloids, such as jatrorrhizine, palmitine, and many others (Fig. 5), have been reported to exhibit antibacterial, antidiabetic, anti-inflammatory, antiulcer, and antifungal properties. They have also been shown to be good for the cardiovascular system (Mfuh and Larionov, 2015; Nyong et al., 2015; Thawabteh et al., 2019; Volleková et al., 2003).

Analysis of the essential oils' composition of *Z. chalybeum* revealed the presence of different chemical substances (Fig. 7), such as α-pinene, β-pinene, sabinene, δ-3-carene myrcene α-terpinene, limonene, 1,8-cineole, γ-terpinene, (*E*)- β -ocimene, p-cymene, terpinolene, 6-methyl-5-hepten-2-one, *trans-p*-menth-2-en-l-ol, citronellal, linalool, terpinen-4-ol, neral, α-terpineol, geranial, geranyl acetate, geraniol, 1,8-cineole, geranial, neral, limonene, linalool, α-terpineol and terpinen-4-ol were the major components (Chisowa et al., 1999).

Mushroom species in buheri wa afya formula

This section covers information available on the mushroom species *G. tsugae* Murrill, the only mushroom species that make up the Buheri wa Afya herbal recipe.

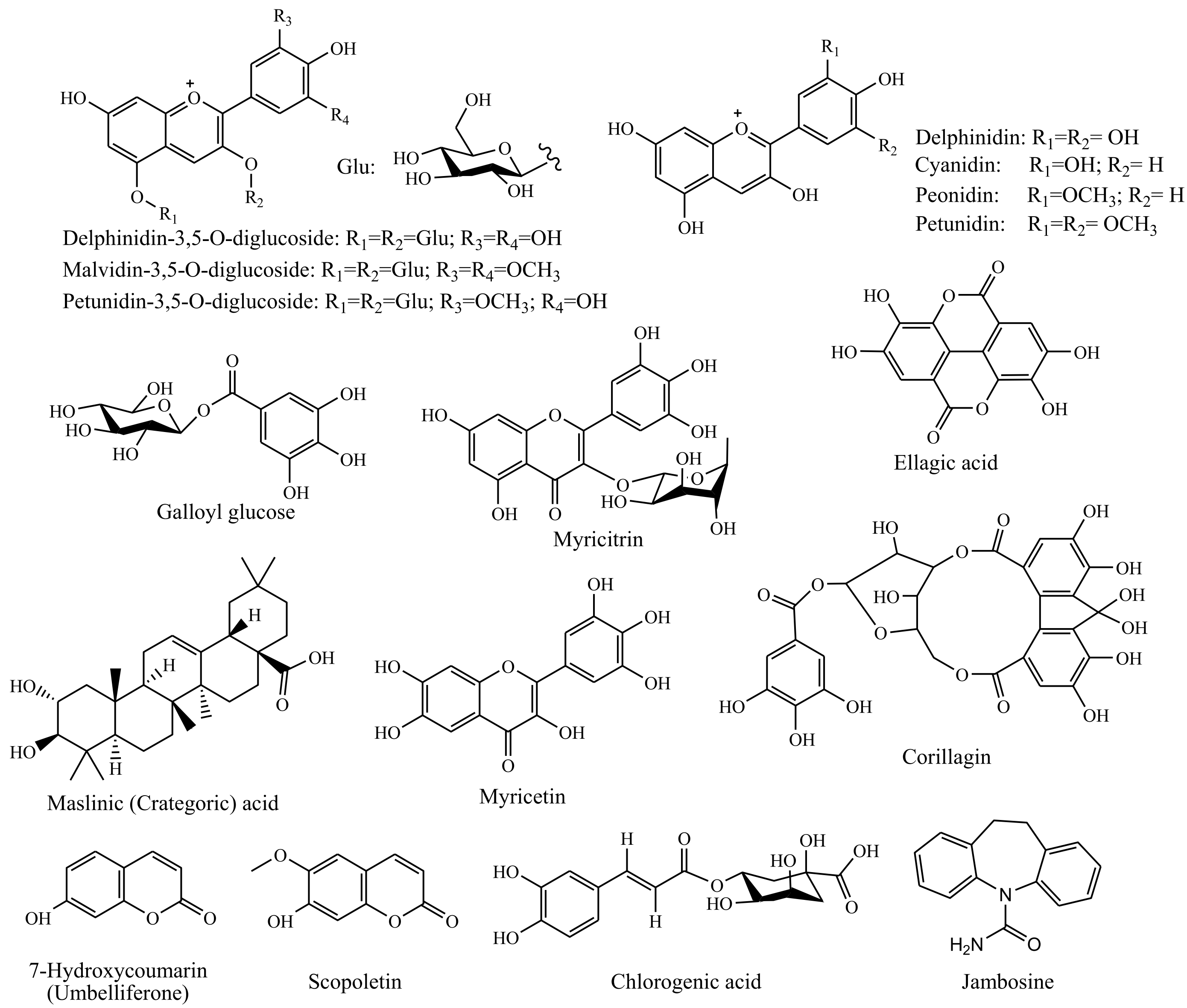

Fig. 4. Some selected phytochemicals from *Syzygiumcumini*.

G. tsugae also known as hemlock varnish shelf or Uyoga mfupa in Swahili, is a flat polypore mushroom of the genus *Ganoderma*, family Ganodermataceae. The genus Ganoderma is among the Basidiomycetes consisting of non-edible medicinal mushrooms because they are naturally very bitter and hard to eat, used in ethnomedicine in the form of extract, tea, or powder (Mshandete, 2014). The genus is also among the common medicinal mushrooms in traditional Chinese medicine and other oriental countries (Ríos et al., 2012; Wei et al., 2009). *G. tsugae* has been reported to be effective in preventing diseases such as hypertension, hypercholesterolemia, cancer (Breene, 1990), and other medicinal roles such as immunomodulatory, liver protective, anti-fibrotic, anti--inflammatory, antidiabetic, antiviral and antimicrobial activities as shown in Table 4 (Paterson, 2006).

In general, *Ganoderma* species are reported to exhibit pharmacological properties as presented in Table 5, including anti-inflammatory (Ko et al., 2008), antitumor (Wang et al., 1993), antioxidant (Mau et al., 2005), and antiviral (e.g., anti-HIV), antibacterial and antiparasitic, blood pressure regulation, cardiovascular disorders, immunomodulating, kidney tonic, hepatoprotective, nerve tonic, sexual potentiator and chronic bronchitis (Wasser and Weis, 1999). G. tsugae has been reported to exhibit mild cytotoxicity against brine shrimp larvae and remarkable antioxidant activities with strong radical scavenging ability (Cao et al., 2018; Gan et al., 1998a; Hsu et al., 2009; Paterson, 2006; Yen, 1999; Yen and Wu, 1999). Furthermore, the *G. tsugae* laccase has been shown to display multifunctional properties like lignin degradation, growth of mycelium, elongation of stipe and pigment production (Tsai et al., 2021). The findings provide scientific support to the ethnomedicine information and the traditional medicinal use of the mushroom (Mshandete, 2014).

The extracts of *G. tsugae* have been reported to contain triterpenoids exhibited both antioxidant, anticancer activities and antihistamine effects (Chen et al., 2015; Yang et al., 2020). The high concentration of phenols in all hot water extracts may be the cause of antioxidant properties of *G. tsugae* (Mau et al., 2005). Sacchachitin, a membrane prepared from the residue of the fruiting body of *G. tsugae* was shown to be able to promote wound healing by inducing cell proliferation, the performance of which sacchachitin membrane as a skin substitute is comparable to the commercial product beschitin (Chuang et al., 2013; Su et al., 1999).

Chemical studies on *G. tsugae* have revealed the presence of lanostane triterpenoids including tsugaric acids, ganoderic acids, tsugariosides, ganodermanontriol, ganodermatriol, ganoderial and many others

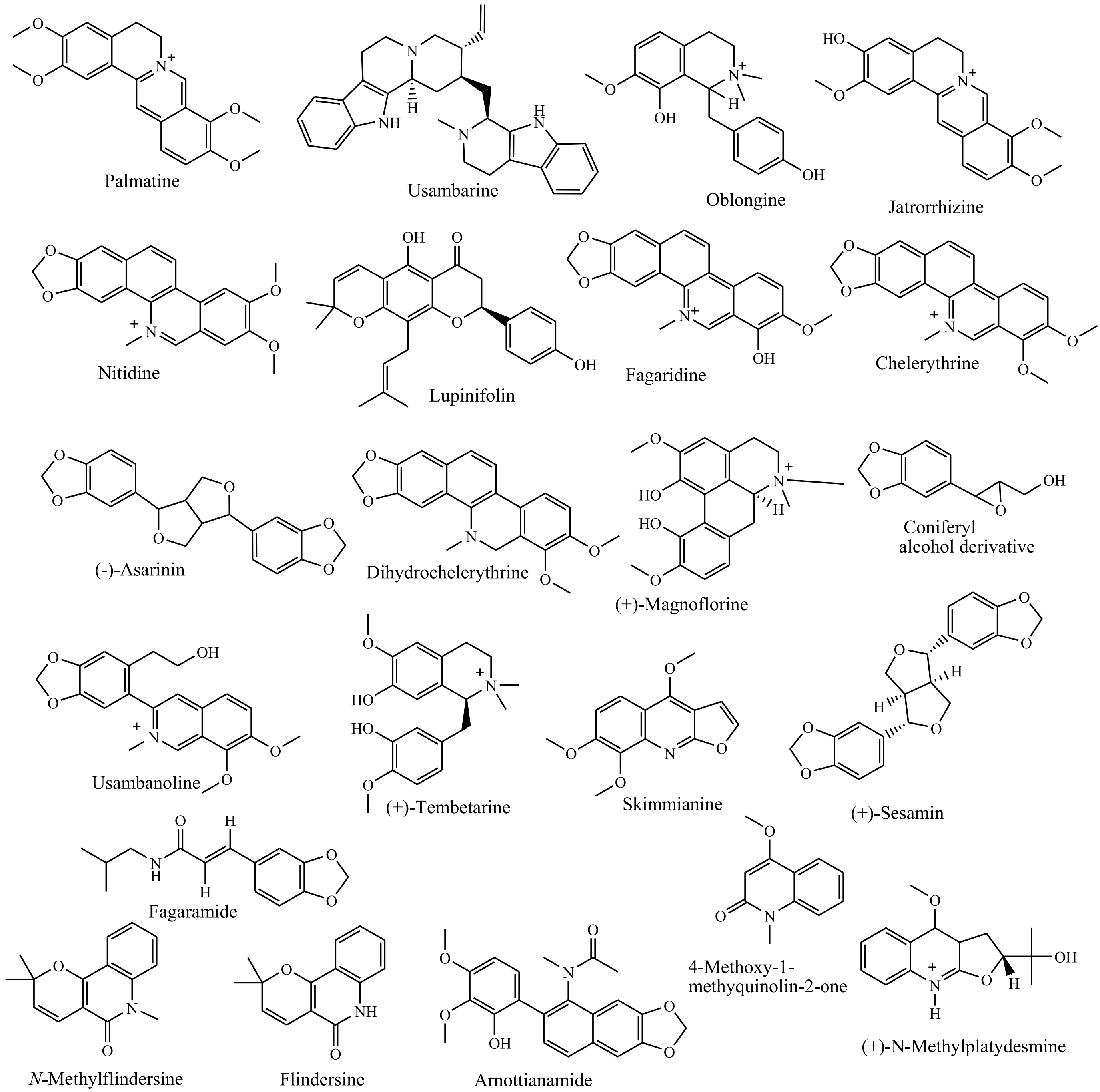

Fig. 5. Selected phytochemicals from *Zanthoxylum chalybeum*.

Table 4
Ethnomedicinal uses of the mushroom species in Buheri wa Afya formula used in the management of COVID-19 in Tanzania.

Fungi Name	Parts used	Ethnomedicinal uses	References
G. tsugae Murrill (Ganodermataceae); Swahili: Uyoga mfupa	Whole	Treatment of hypertension, cancer, hypercholesterolemia, anti-fibrotic, immunomodulatory, liver protective, anti-inflammatory, antidiabetic, antiviral and antimicrobial activities, sexual potentiator.	(Arunachalam et al., 2022; Breene, 1990; Chun et al., 2021; Konusova et al., 2021; Mirończuk-Chodakowska et al., 2021; Mshandete, 2014; Paterson, 2006)

as presented in Table 6 (Gan et al., 1998; La Clair et al., 2011; Lin et al., 1997, 2016; Su et al., 1999; Wang et al., 1993; Wei et al., 2009). Furthermore, a palmitamide was also reported to occur in the mushroom (Lin et al., 2016). Fig. 6 presents some of the selected compounds isolated from *G. tsugae*.

Different studies have reported the potentials of using mushrooms as therapeutics or preventatives against COVID-19. The characteristics might be related to the presence of beta-glucans, a type of naturally

Table 5
Phamacological properties of the mushroom species in Auheri wa Afya formula used in the management of COVID-19 in Tanzania.

Fungi name	Parts used	Ethnomedicinal uses	References
G. tsugae Murrill (Ganodermataceae); Swahili: Uyoga mfupa	Whole	Anti-inflammatory, antitumor, and antioxidant, antiviral, (e.g., anti-HIV), antibacterial and antiparasitic, blood pressure regulation, cardiovascular disorders, immunomodulating, kidney tonic, hepatoprotective, nerve tonic, and chronic bronchitis.	(Arunachalam et al., 2022; Chen et al., 2015; Chuang et al., 2013; Chun et al., 2021; Gan et al., 1998b; Ko et al., 2008; Konusova et al., 2021; La Clair et al., 2011; Mau et al., 2005a, 2005b; Mirończuk-Chodakowska et al., 2021; Mshandete, 2014; Paterson, 2006; Ríos et al., 2012; Su et al., 1999b; Tsai et al., 2021; Wang et al., 1993; Wasser and Weis, 1999; Wei et al., 2009)

Table 6
Chemical composition of the mushroom species in Buheri wa Afya formula used in the management of COVID-19 in Tanzania.

Species name	Chemical composition	References
G. tsugae Murrill (Ganodermataceae); Swahili: Uyoga mfupa	*β*-carotene, lycopene, lanostane triterpenoids: including tsugaric acids, ganoderic acids, tsugariosides, ganodermanontriol, ganodermatriol, ganoderial, lucidone, lucidenic acid, *β*-D-glucan, triterpenes.	(Chung et al., 1997; Chen et al., 2015; Chuang et al., 2013; Gan et al., 1998; Ko et al., 2008; La Clair et al., 2011; Lin et al., 1997, 2016; Ríos et al., 2012; Su et al., 2000; Wang et al., 1993; Wei et al., 2009)

occurring polysaccharide well-known for their immunological and metabolic regulating functions, including anticancer, antibacterial, and antiviral actions. *β*-glucans may be used to treat and prevent COVID-19, according to new research. Other mycochemicals, such as terpenoids, alkaloids, flavonoids, phenols, tannins, and polyphenols, as well as proteins, lipids, and peptides, have also been reported in mushrooms (Chung et al., 1997; Arunachalam et al., 2022; Chun et al., 2021; Konusova et al., 2021; Mirończuk-Chodakowska et al., 2021).

Discussion

The review of the plant and mushroom species in buheri wa afya formula has revealed details on the ethnomedicine applications of the species for the prevention and treatment of COVID-19 and other viral infectious diseases, as well as their chemical composition and related biological properties (Aini et al., 2022; Arunachalam et al., 2022; Chun et al., 2021; Evariste, 2020; Innocent et al., 2022; Konusova et al., 2021; Malabadi et al., 2021; Mirończuk-Chodakowska et al., 2021; Nakaziba et al., 2021; Raimi et al., 2022; Renjana et al., 2021; Shaffique et al., 2021). Through this review, information about the ethnomedicine usage of the five plant species in Buheri wa Afya for the treatment of COVID-19 and other viral infections in India and Africa has been reported in the literature. These plant species have been reported to exhibit anti-inflammatory, antiviral, antibacterial, anticancer, antitumor, and immunomodulatory properties that aid in the fight against the disease. The presence of bioactive compounds such as flavonoids, phenols, alkaloids, vitamins, macro- and micronutrients, metabolites, amino acids, vitamin C, zinc, and protein contents may be associated with the therapeutic properties of the plant species against COVID-19. Additioanlly, among the ingredients of the buheri wa afya formula is a mushroom, *G. tsugae*. Mushrooms have been reported to play vital role in the treatment of many ailments in Chinese traditional medicine for a very long time. Recently, mushrooms have been reported to have potentials in the prevention and treatment of COVID-19. Various biologically active compounds, such as *β*-glucans, lanostane triterpenoids, mushroom polysaccharides, and many more have been obtained from *G. tsugae*. The reported biological activities of the constituents of the formula, such as antiviral, antioxidant, immunomodulatory, neuroprotective, and antithrombotic properties, among others may be associated with effectiveness of buheri wa afya in the management and treatment of COVID-19 and other viral infectious disease. Furthermore, the findings offer scientific support on the use of the formula in the treatment of COVID-19.

The review also revealed the presence of different compounds which belong various chemical classes like phenolics, alkaloids, terpenoids, coumarins, catechins, and vitamins, with a wide range of biological activities, including anti-inflammatory, immunomodulating, antiviral, antitumor, and many others. These properties could be directly associated with the efficacy of the therapeutic herbs in the fight against COVID-19 and associated symptoms.

All plant species reported in this study, with the exception of the mushroom, *G. tsugae*, contained flavonoids. Some of the flavonoids encountered throughout this review are quercetin, kaempferol, luteolin, glycosides of quercetin and kaempferol and the tilirosides (Fig. 1). Flavonoids have been reported to have ability to bind to the spike protein, their efficacy against the H5N1 avian influenza virus, and their ability to inhibit SARS-CoV papain protease (PLpro) make them potential lead compounds for the treatment of COVID-19 and other viral infectious disorders (Cho et al., 2013; Jahan and Onay, 2020; Kaul et al., 2021; Lima et al., 2021; Sun and Shahrajabian, 2023).

Coumarin derivatives such as scopoletin have also been reported to occur in the plant species under review. Compounds belonging to this class have been reported to demonstrate wide range of pharmacological properties such as anti-inflammatory, anticoagulant, antibacterial, antifungal, antiviral, anticancer, antihypertensive, antitubercular, anticonvulsant, antiadipogenic, Cytochrome P450 inhibiting, antihyperglycemic, antioxidant, and neuroprotective activities (Jung and Park, 2009; Kirkiacharian et al., 2008; Luchini et al., 2008; Matos et al., 2015; Sarker and Nahar, 2020; Semwal et al., 2020). Among the coumarins, 4-hydroxycoumarin [DB03410] has been reported to be used as an anticoagulant, which is critical in the management of thrombotic complications related to COVID-19 (Jung and Park, 2009; Kirkiacharian et al., 2008; Luchini et al., 2008; Matos et al., 2015; Sarker and Nahar, 2020; Semwal et al., 2020).

Other groups of phenolic compounds reported to occur in the species under review are the catechins, procyanidins (Dasiman et al., 2021; Osakabe et al., 2022; Rauf et al., 2019), xanthones (Dibwe et al., 2014a, 2014b, 2014c, 2012), cyanidins and anthocyanins (Ayyanar and Subash-Babu, 2012; Chhikara et al., 2018; Uddin et al., 2022). This group of compounds have been reported to possess varieties of pharmacological properties, including antioxidant, antitumor, antiallergic, anti-inflammatory, antibacterial, antifungal, and antiviral activities (Chen et al., 2022; Dasiman et al., 2021; Khoo et al., 2017; Liang et al., 2021; Osakabe et al., 2022; Rauf et al., 2019), whereas cyanidins and anthocyanidins are reported to possess anti-inflammatory, anticancer, antidiabetic, antitoxicity, cardiovascular, and nervous protective capacities, antimicrobial and anti-obesity effects, as well as prevention of cardiovascular diseases (Khoo et al., 2017; Liang et al., 2021). They have also been reported to exhibit immunosuppressive, and antiallergy properties and protected against chronic diseases and metabolic disorders. They may protect against chronic diseases such as cardiovascular, cancer, and immune-related diseases. The anti-inflammatory activity is due to their ability to inhibit adipogenesis, melanogenesis, oxidative stress, and enhancement of lipid metabolism and macrophage activity

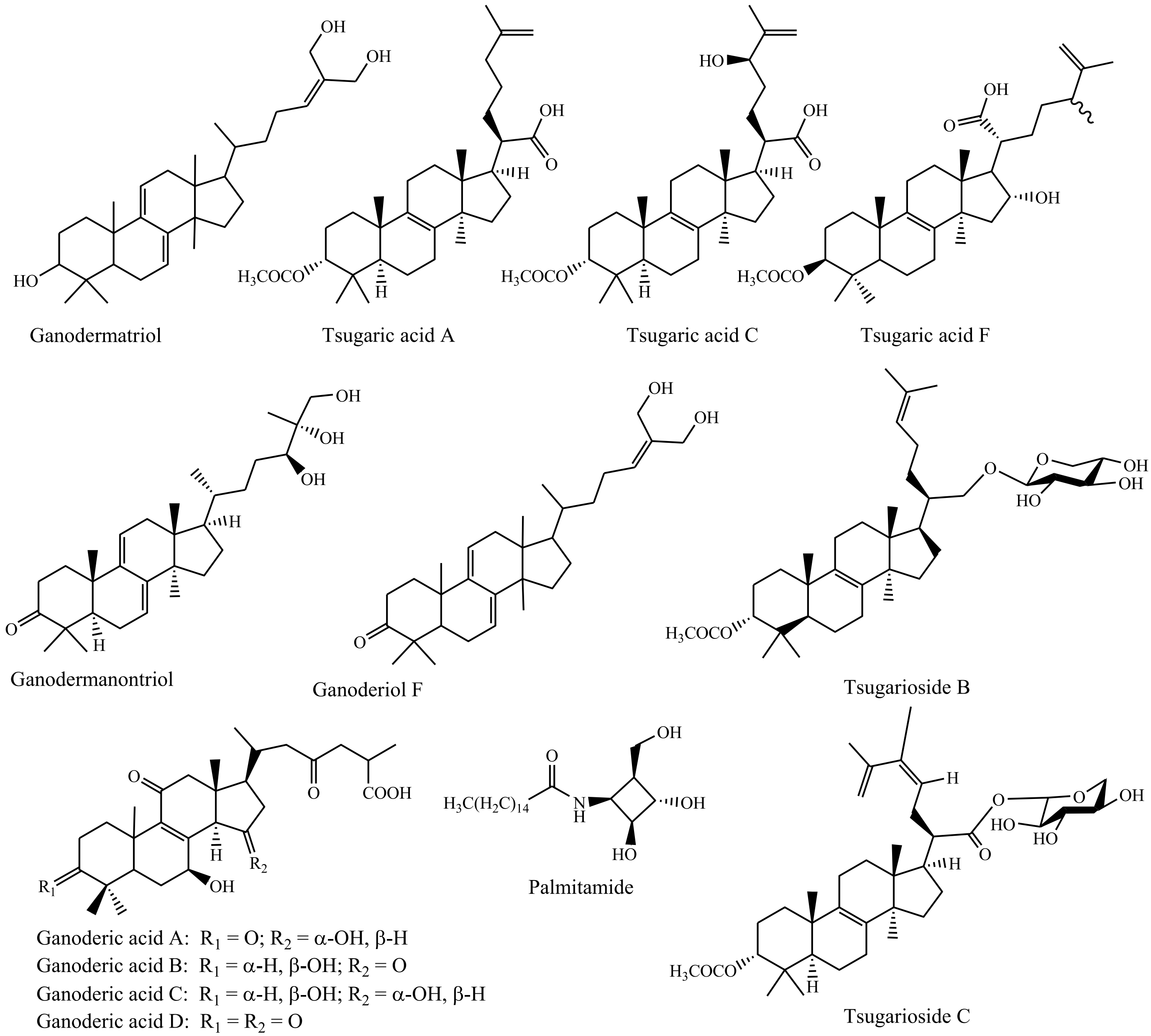

Fig. 6. Secondary metabolites isolated from *Garnoderma tsugae*.

(Ayyanar and Subash-Babu, 2012; Chen et al., 2022; Chhikara et al., 2018; Khoo et al., 2017; Liang et al., 2021; Uddin et al., 2022).

Different classes of terpenoids ranging from monoterpenes to triterpenes with diverse structures have been reported to occur in the plant species under review, which include sterols, saponins, limonoids, pentacyclic terpenoids and essential oils to occur in the species. These compounds have been shown to have various pharmacological properties, such as antitumor, antioxidant, anti-inflammatory, antibacterial, antiviral, antimalarial effects, promote transdermal absorption, prevent and treat cardiovascular diseases, anticancer, antidiabetic, neuroprotective, antimicrobial and immunomodulatory, and antiviral activities including SARS-CoV-2 (Alqahtani et al., 2013; Ashour et al., 2019; Bahbah et al., 2020; Banerjee et al., 2019; Farmanpour-Kalalagh et al., 2022; Ghante and Jamkhande, 2019; Graebin, 2018; Kareem et al., 2022; Khumalo et al., 2019; Lyu et al., 2021; Yang et al., 2020). In addition, insect resistance, immunoregulation, antioxidation, antiaging, and neuroprotection have also been reported for the terpenoids. They have also been shown to have the ability to decrease blood lipids, lower cancer risks, and lower blood glucose response. Saponins may also inhibit the cellular attachment, entry, adsorption, and penetration of a virion into the host cell, hence may have a role in curing COVID-19 patients (Farmanpour-Kalalagh et al., 2022).

Alkaloids encountered in this study have been reported to possess anti-inflammatory, anticancer, analgesics, local anesthetic and pain relief, neuropharmacologic, antimicrobial, antifungal, and many other activities (Anza et al., 2022; Kamikawa et al., 1996; Krane et al., 1984; Kurek, 2019; Lúcio et al., 2015). The alkaloids reported from the species under review, have promising pharmacological properties, including analgesic, anti-inflammatory, anticancer, antidiabetic, antimicrobial, antifungal, antihyperlipidemic, cardioprotective, memory enhancement, antidepressant, antioxidant, antinociceptive, antimicrobial, anti-HIV and cholesterol lowering effects (Anza et al., 2022; Kamikawa et al., 1996; Krane et al., 1984; Kurek, 2019; Lúcio et al., 2015).

The information gathered from this study for the constitutents of Buheri wa Afya formula confirms the effectiveness of the formula in managing COVID-19, thus supporting the use of the formula for the

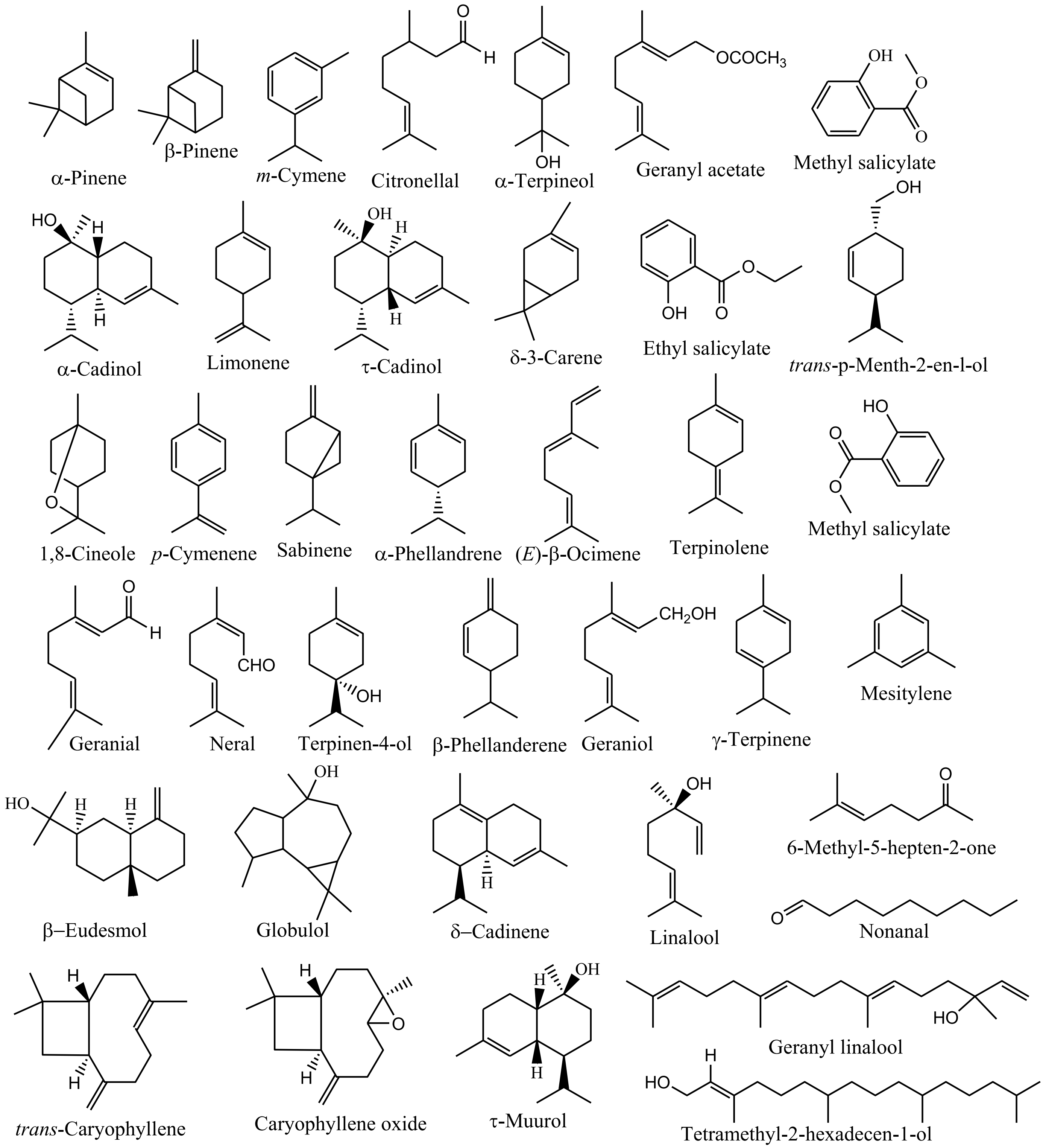

Fig. 7. Selected essential oil constituents from the plants and mushroom species.

management of the pandemic.

Conclusions

This review of the plant and mushroom species has demonstrated the potential of the ingredients of Buheri wa Afya as an effective remedy for the treatment of COVID-19 and other viral infectious diseases. The inherent antioxidant, anti-inflammatory, antiviral, and immunomodulating qualities of the ingredients in the Buheri wa Afya recipe explain why it has been found to be effective in preventing, reducing symptoms, and curing COVID-19 in Tanzania. Furthermore, the review has demonstrated the importance of indigenous knowledge in managing a range of health issues and promoting healthy living. The deadly COVID-19 outbreak has further highlighted how much the people of Tanzania, African, and other countries rely on medicinal plants and mushroom species as the most effective alternative for the management of a variety of health issues.

From the literature findings, there is a need for more concerted efforts in the exploration of fungi, shrubs, and higher plants which are used the fight against COVID-19 and other diseases, as well as the significance of identifying and preserving Tanzania's rich ethnomedicine knowledge of herbal medicine as well as knowledge of herbal medicine throughout the world where it is applicable. The isolation and identification of the active compounds that can be employed as lead compounds in the development of more effective and secure drugs for the treatment of COVID-19, viral infections, and other pandemic diseases is also essential.

CRediT authorship contribution statement

John J. Makangara: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Anthony M. Mshandete:** Investigation, Writing – review & editing. **Ernest R. Mbega:** Investigation, Writing – review & editing. **John R. Nyika:** Investigation, Writing – review & editing. **Frank Mbago:** Investigation, Writing – review & editing. **Edward G. Ndilanha:** Investigation, Writing – review & editing. **Raphael J. Nyika:** Investigation, Writing – review & editing. **Joseph J. Nyika:** Investigation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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