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REVIEW ARTICLE

The use of black pepper (*Piper guineense*) as an ecofriendly antimicrobial agent to fight foodborne microorganisms

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Abstract

Consumers demand clean-label food products, necessitating the search for new, natural antimicrobials to meet this demand while ensuring food safety. This review aimed at investigating the antimicrobial properties of black pepper (*Piper guineense*) against foodborne microorganisms. The existence of foodborne illness, food spoilage, food waste, the resulting negative economic impact of these issues, and consumer interests have all pushed the food industry to find alternative, safe, and natural antimicrobials to be used in foods and beverages. Consumers have also influenced the demand for novel antimicrobials due to the perceived association of current synthetic preservatives with diseases and adverse effects on children. They also have a desire for clean-label products. These combined concerns have prompted researchers at investigating plant extracts as potential sources for antimicrobials. Plants possess many antimicrobial properties; therefore, evaluating these plant extracts as a natural source of antimicrobials can lead to a preventative control method in reducing foodborne illness and food spoilage, inclusively meeting consumer needs. In most regions, *P. guineense* is commonly utilized due to its potent and effective medicinal properties against foodborne microorganisms.

Keywords Antimicrobial agents · Food · Health · Microorganisms · *Piper guineense*

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Introduction

Consumers have questioned the effects of food and diet on behavior and health since as early as 1922 (Shannon 1922). The Center for Disease Control and Prevention (2018) estimated that each year in the USA over than 48 million people fall ill from foodborne diseases, resulting in approximately 130,000 hospitalizations and 3,000 deaths (CDC 2018). Recent annual surveillance reports published by the CDC (2015) stated that the bacterial pathogens responsible for the most outbreak-related illnesses and hospitalizations were *Salmonella* and shiga toxin-producing *Escherichia coli.*

Although foodborne diseases have negative effect on foods, food spoilage by microorganisms is considered an important issue and can be a problem. Bacteria and fungi can cause food spoilage by degrading nutrients and/or altering desired organoleptic characteristics (Negi 2012; Isikhuemen et al. 2020). The current alternative methods for controlling foodborne illness and spoilage are acidification, pasteurization, ultra-high temperature treatments, fermentation, storage temperature control, and the addition of several natural and synthetic antimicrobials. However, these current methods of control inadequately control all microorganisms as proven by continued spoilage issues and foodborne disease outbreaks (Negi 2012; Davidson et al. 2013; Kambiré et al. 2019; Abd El-Hack et al. 2020a, 2021a; El-Tarabily et al. 2021).

The consumer demand for more natural foods has led to studies utilizing more naturally derived means of food preservation. In the United States, there is a growing popularity for fast, ready-to-eat foods, which are more susceptible to microbial contamination (Ahn et al. 2007). Therefore, controlling both contamination and spoilage of these products through natural antimicrobials is increasingly vital. Although these additives are considered safe by the Food and Drug Administration (FDA), consumers are worried about the long-term effects of accumulation in the body and the sensitivity to children (Rosati and Saba 2004; Kambiré et al. 2019). Nitrates and nitrites, benzoates, sorbates, and sulfites are commonly controversial additives (Sharma 2015), with each linked to various dangerous and serious conditions, namely migraines, stomach cancer, asthma, and attention deficit disorders (Rosati and Saba 2004).

The medicinal plant Ashanti pepper or African black pepper (*Piper guineense* Schumach & Thonn), is used worldwide. It is ubiquitously recognized due to its well-established therapeutic properties as the cure for many bacterial diseases (Ene-Obong et al. 2018; Isikhuemen et al. 2020). Economically, *P. guineense* is a spice that is mostly used in flavoring local dishes in West African countries, and the fruits are sold in local markets as condiments. It is a medicinal plant that has been conventionally used in the cure of several ailments and infectious diseases, including rheumatoid arthritis, diarrhea, bronchitis, cough, intestinal diseases, stomach ache, and asthma (Konning et al. 2004; Ogunniran 2009; Gbekley et al. 2017; Amadi et al. 2019). Furthermore, *P. guineense* is used to treat mental disorders, febrile convulsions fever, and to enhance fertility in females (Oyemitan et al. 2015). In the cure and prognosis of liver diseases, it is highly effective due to its high antioxidant effects (Oyinloye et al. 2017; Ehimemen and Salisu 2020). In preparing postpartum soup for women after childbirth, the leaves, seeds, and fruits are used as they are believed that to help in the contraction of the uterus and cleaning of women's womb of possible remaining placenta after childbirth and enhance breast milk production (Ene-Obong et al. 2018; Ehimemen and Salisu 2020).

Further discussing its beneficial impacts, Uhegbu et al. (2015) reported that it raises the blood hemoglobin concentration by positively influencing red and white blood cell counts. Biological studies have shown that *P. guineense* extracts possess antifungal and antibacterial properties (Okeke et al. 2001; Konning et al. 2004; Tekwu et al. 2012). It has been noted that *P. guineense* extracts exhibit antifungal effects, making this a modern non-conventional antifungal drug (Ngane et al. 2003; Kambiré et al. 2019).

Additionally, studies showed that dietary *P. guineense* successfully inhibited the growth of *Mycobacterium tuberculosis*, a primary cause of tuberculosis which is predominent in different developing nations (Tekwu et al. 2012). Essential oils and extracts of *P. guineense* possess anticonvulsant, hypothermic, sedative, muscle relaxant, antipsychotic, and anticonvulsant properties (Oyemitan et al. 2015). Extracts and essential oils also have antioxidant and antidiabetic activities and can be used to treat depression (Oboh et al. 2013; Okon et al. 2013; Oyemitan et al. 2015; Amadi et al. 2019). *P. guineense* contains valuable bioactive compounds that could serve as therapeutic agents for drug discovery (Mgbeahuruike et al. 2017), and these bioactive compounds such as alkaloids and amides were reported to be present in various parts of the plant (Adesina et al. 2003; Scott et al. 2005; Isikhuemen et al. 2020).

Apart from its antibacterial and antifungal properties, *P. guineense* extracts and bioactive compounds were reported to exhibit anticancer and antitumor efficacy and could be a potential lead to the discovery of new anticancer drugs (Bezerra et al. 2005; Iweala 2015). It also contains piperine, which is an alkaloid with interesting pharmacological properties that have been reported to have antibacterial, antifungal, and anticancer properties, including being capable of enhancing the effectiveness of antimicrobials and

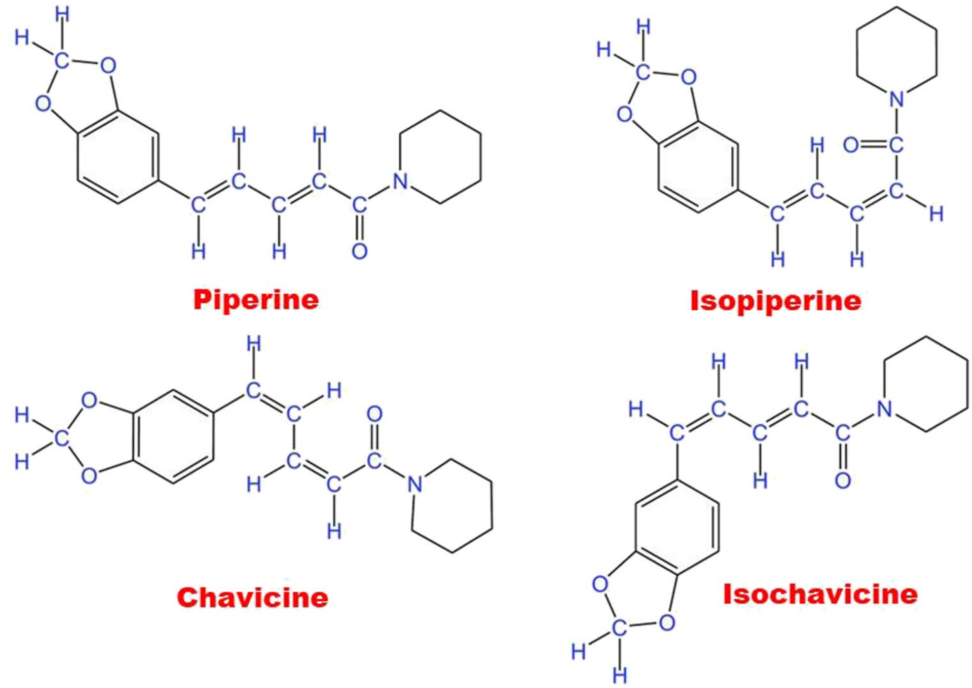

Fig. 1 The chemical structures of piperine and its analogs (Ravindram, 2000; Peter 2006)

chemotherapeutic drugs (Bezerra et al. 2006, 2008; Imo et al. 2018; Nageswari et al. 2018). The chemical structures of piperine and its analogs are represented in Fig. 1.

Reports have shown that *n*-hexane, methanol, ethanol, and chloroform fractions of the leaf and fruit of *P. guineense* have impressive antibacterial and antifungal properties. Moreover, metabolites from *P. guineense* such as piperine and piperlongumine (also called piplartine or piperlongumin) have also been found effective in controlling fungal pathogens such as *Candida albicans*. Therefore, *P. guineense* can be used as a traditional medicine to control several pathogenic fungi. Furthermore, piperamide mixtures may be employed as a helpful tool in producing novel antibacterial and antifungal preparations to depress infectious agents (Imo et al. 2018). In this review, we focused on the use of *P. guineense* as an effective agent against foodborne microorganisms due to its promising antimicrobial and medicinal properties.

Examples of some common foodborne microorganisms

The most common foodborne microorganisms were *Listeria monocytogenes*, *Escherichia coli*, *Salmonella enterica* serovar *typhi*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus subtilis*, *Lactobacillus fermentum*, *Vibrio parahaemolyticus*, and *Saccharomyces cerevisiae*. Strains of each microorganism were selected based on their association with foodborne illness, outbreaks, or food spoilage.

Although antibiotics have been widely used in agriculture and aquaculture to boost growth and prevent diseases resulting from microorganisms, their widespread use has played a vital role in microbes and its antibiotic resistance. Therefore, natural antibiotic alternatives have become a necessity to overcome antibiotic-resistant microorganisms, including natural products (Abdelnour et al. 2020b; El-Saadony et al. 2020, 2021a, 2021b; Alagawany et al. 2021b), probiotics (Abd El-Hack et al. 2020b, 2021d; El-Saadony et al. 2021d), prebiotics (Yaqoob et al. 2021), essential oils, organic acids (Abd El-Hack et al. 2021c), and medicinal plants (Abou-Kassem et al. 2021; Saad et al. 2021).

Listeria monocytogenes

L. monocytogenes is a Gram-positive bacterium that is ubiquitous in nature, and is found in sewage, water, and soil. It is often present where lactic acid bacteria (LAB) are active, which is the cause of the high number of *Listeria* outbreaks in dairy products. When ingested orally, it propagates in the intestinal tract, where it penetrates the tissue and circulates in the blood stream (Jay et al. 2005a).

This bacterial pathogen is specifically dangerous for pregnant women, due to its ability to cross into the placenta and cause abortion or stillbirth. It can withstand different temperatures (1–49 °C) and pH (4–9) (Jay et al. 2005a). The United States, compared with other countries, such as the UK and Austria, has strict policies when it comes to the presence of this bacterium in foods. They have no allowable limits, and any *L. monocytogenes* detected in foods is considered an adulterant, subjecting the product in question to recalls and public warning (Jay et al. 2005a).

Escherichia coli

E. coli was first recognized as a Gram-negative foodborne pathogen in 1971, in the United States, with over than 200 known serotypes. The main serotypes known to be the most dangerous is *E. coli* O157:H7 and the non-O157 STEC strains. Due to the prevalence of the non-O157 strains in foodborne outbreaks, the Food Safety and Inspection Service named the dangerous non-O157 strains the "Big 6" (USDA 2010).

Enterohemorrhagic *E. coli* O157:H7 (EHEC) is classified as one of the most dangerous strains of *E. coli* because it produces shiga-like toxins that lead to severe toxic infections. It can survive in foods at a low pH for an extended period and is most commonly found in beef more than any other food source; however, it is still of concern in other meat, poultry, seafood, and fresh crops. *E. coli* is also one of the principal reasons for traveler's diarrhea, and acute watery diarrhea. This is common for travelers to encounter when first entering a foreign country (Jay et al. 2005b; El-Saadony et al. 2021c).

In 2017, an occurrence of *E. coli* STEC O157:H7, the shiga toxin-producing strain, was identified in healthy brand soynut butter and was isolated from unopened containers during laboratory testing (CDC 2017a). There have been 32 reported incidences in 12 different states associated with this outbreak while being tracked from January to April 2017. There was a major recall of this product; however, due to its potential for such a long shelf life, others may still be affected in the future if they were not made aware of the recall. It was discovered that 81% of the total people affected were under 18 years of age (CDC 2017b).

Salmonella enterica

Salmonella is another foodborne pathogen of great concern. Similar to *E. coli*, it is Gram-negative bacterium with similar growth properties. Over 2,000 serovars of *Salmonella enterica* have been identified. *Salmonella* often colonizes mammals and birds (McClelland et al. 2001; Reda et al. 2020, 2021a, 2021b; Sheiha et al. 2020; Abd El-Hack et al. 2021b).

To be infected by this pathogen from foods, a significant number of cells must be ingested. Improper handling and preparation of foods contribute to the concern of this pathogen in homes and in the food-service industry (Jay et al. 2005c). According to the foodborne illness outbreak surveillance program, FoodNet, in 2016, *Salmonella* was one of the reported two pathogens that caused the highest incidence of foodborne illnesses, matching the data reported in 2015.

Staphylococcus aureus

S. aureus is the popular strain of *Staphylococcus* involved in foodborne outbreaks. It is a Gram-positive bacterium that requires specific organic compounds for growth, such as amino acids for nitrogen sources and B vitamins. It causes gastroenteritis by ingesting foods that contain enterotoxins produced by the bacterium. The known hosts for *S. aureus* are humans and other domestic animals (Bennett et al. 2013).

Generally, low numbers have been found in almost all food products that humans have handled unless a heat processing step has been applied during production. *S. aureus* cells, in comparison to enterotoxins, are much more sensitive to heat. The foods most commonly associated with an outbreak of disease caused by this bacterium are meat and poultry dishes (Bennett et al. 2013). The outbreaks for this microorganism are most commonly associated with unhygienic foods and improper refrigeration of foods after being prepared (Jay et al. 2005d).

Enterococcus faecalis

E. faecalis is a Gram-positive bacterium commonly found in fecal matter due to its presence in the natural gut microflora (Abdelnour et al. 2020a; Ashour et al. 2020; Alagawany et al. 2021a). It is of great significance due to its sanitation practices because of its growing resistance to antimicrobials. Although it was used as a fecal indicator of water due to its similarities with coliforms, it is generally less numerous. It is a bacterium that requires specific organic material for growth, specifically, the vitamin B complex family and certain amino acids. It can grow at a much wider range of pH levels than any other foodborne pathogens. It grows under harsh environments, such as low oxidation–reduction (Eh) potential, thus leading to its microaerophilic classification (Jay et al. 2005e).

Most enterococci are generally not regarded as foodborne pathogens; however, they can be acquired through food consumption. They also cause food intoxication by producing biogenic amines consumed by humans (Oprea and Zervos 2007). Enterococci are also linked to food spoilage. High levels of this bacterium in cheese often lead to deterioration of sensory characteristics in cheese products. Due to this microorganism's thermal resistance, it survives pasteurization and persist into the next stage of cheese making (Giraffa 2003).

Bacillus subtilis

Bacillus is a spore forming, Gram-positive bacterium with varying degrees of harm, based on the strain. Some strains of *B. subtilis* are often used in fermented foods, such as tofu and as a bacterial component in probiotics (Inatsu et al. 2006; Hong et al. 2008; Patel et al. 2009). Another species of this microorganism, *Bacillus cereus*, is highly associated with foodborne illness due to its production of enterotoxins (Hong et al. 2008). In 1993, 14 people were infected by *B. cereus*; however, the pathogenic bacterium failed to cause any death (CDC 1994).

In the USA, the leading food found to contain *B. cereus* was fried rice, due to the presence of this bacterium in the uncooked rice. The spores produced by this bacterium are typically heat resistant and will be passed onto foods (Terranova and Blake 1978; CDC 1994). *B. subtilis* is highly characterized and has a genome similar to most other Gram-positive bacteria, making it an excellent model bacterium for microbiological testing (Borriss et al. 2018).

Lactobacillus fermentum

L. fermentum is an anaerobic, Gram-positive lactic acid-producing bacteria. It is often linked to its potential use in probiotics and other food supplements (Ramos et al. 2013; El-Saadony et al. 2021e). The characteristics that make *L. fermentum* applicable as a probiotic, include acid tolerance, adherence to epithelial cells and tissues, and the potential to influence bacterial adhesion activity (Del Re et al. 2000; Ramos et al. 2013).

Lactobacillus spp. have been considered as leading fermenting Gram-positive bacteria, and their role in winemaking is acknowledged. They are liable for the step called malolactic fermentation (MLF) and, if uncontrolled properly, can lead to unwanted metabolic activity. Once this step is complete, sulfate is added to halt fermentation, as over fermentation will lead to undesired organoleptic characteristics (García-Ruiz et al. 2012).

LAB are used in food preservation. LAB can produce lactic acid, creating undesirable conditions for spoilage microorganisms to grow and reproduce (Gerez et al. 2013). The functional components of LAB that make it a strong antimicrobial agent are flavoproteins and peroxidases. While in the presence of oxygen, they produce hydrogen peroxide, resulting in strong oxidation potential and destruction of cellular functions (Gerez et al. 2013).

Vibrio parahaemolyticus

V. parahaemolyticus is a Gram-negative halophilic bacterium that has a much shorter generation time than the aforementioned bacteria, requiring high amounts of salt to survive. It infects shellfish in coastal ocean waters (Bartley and Slanetz 1971).

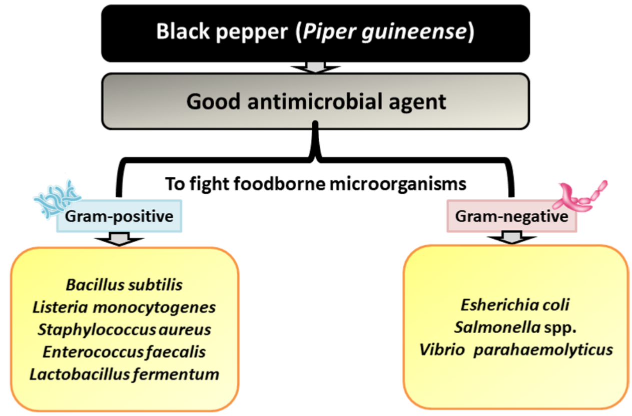

Fig. 2 Black pepper (*Piper guineense*) is a good antimicrobial agent to fight foodborne microorganisms

The average generation period of *V. parahaemolyticus* is 12–14 min as compared to *E. coli*, which has an average generation time of 16 to 17 min at an optimum growth temperature of 37 °C (Ulitzur 1974). Seafood such as oysters, clams, crab, and other similar crustaceans are the leading cause of outbreaks and the primary carrier of the pathogenic forms consumed by humans; while cross-contamination is the second leading cause (Beuchat 1982).

There are worldwide reports of foodborne outbreaks; however, it remains a significant issue in Asian countries such as Japan and Taiwan (Lin and Schwarz 2003). There was an outbreak in 2013 in the United States associated with this bacterium due to the consumption of shellfish from various Atlantic harvesting zones that affected over 100 people, causing 6 to be hospitalized (CDC 2013).

Saccharomyces cerevisiae

This specific strain of yeast is often referred to as bakers' or brewers' yeast due to its strong fermentation abilities and acid tolerance. It is frequently used in bread, beer, and wine production, as well as other various fermented food products (Jay et al. 2005f). The primary functions during fermentation are alcohol production, aroma development, stimulating LAB, fortifying nutrients, and inhibiting mold growth (Jespersen 2003).

It is rarely responsible for spoilage in various foods; however, it has been linked to the spoilage of fruit juices and can lead to the over fermentation of beverages (Parish 1991). It has been shown that contamination of juice products can be linked to the presence of yeast cells on the outside of the fruits during processing (Iqbal et al. 2016).

Roles of *Piper guineense* in reducing foodborne microorganisms

Black pepper is an excellent antimicrobial agent that can be used to fight foodborne microorganisms (Fig. 2). *P. guineense* is usually consumed in Nigeria due to its potent and effective medicinal properties. It has been used to treat illnesses ranging from dysentery to bronchitis. Both bactericidal and bacteriostatic properties have been reported for this plant, which are traced back to the high concentrations of potent secondary metabolites in the leaves and seeds (Okigbo and Igwe 2007; Ogunniran 2009).

The secondary metabolites significant in this extract are alkaloids, reducing sugars, tannins, and saposins (Konning et al. 2004). Ethanolic and methanolic extractions of this crude plant extract have better antimicrobial activity compared to an aqueous plant extract. This is due to the solvents abilities to extract more phytochemicals from the plant matter (Konning et al. 2004; Nwinyi et al. 2008; Ehimemen and Salisu 2020). Reports from various tests showed that this plant possesses high broad-spectrum antimicrobial activity against fungi and bacteria such as the Gram-positive bacterial species, primarily *B. subtilis* and *S. aureus*. Moreover, this herb has also controlled the virulence of fungi (*Aspergillus* and *Candida*) (Konning et al. 2004; Nwinyi et al. 2008).

P. guineense is a perennial spice plant from the genus piper encompassing heart-shaped leaves and entitled among the major herb plants, widely distributed in many parts of Africa (Oyemitan et al. 2015). This perennial climbing plant belongs to the Piperaceae family, which is mainly grown for its fruits, leaves, and roots. It grows up to 20-m height, climbing by employing its adventitious roots (Besong et al. 2016). It has various parts, which are used for different medicinal purposes. It consists of black-berry fruits, seeds, leaves, rhizomes, and flower buds (Besong et al. 2016). The fruits are sold in markets as flavoring agents (Freiesleben et al. 2015; Kambiré et al. 2019). Its other names, include Guinea pepper, Benin pepper, false cubeb, and Ashanti pepper (Besong et al. 2016). Pepper has multiple species with reports to have varying chemical constituents based on their diverse nature (Oyemitan et al. 2015; Besong et al. 2016; Ehimemen and Salisu 2020). Species found in the same geographical region could have variations in their chemical constituents. It is a vegetable plant that enhances the taste of food (Ehimemen and Salisu 2020).

Traditional medicine plants

West Africa is a region abundantly rich in therapeutic plants which are used to cure infectious diseases (Oguntibeju 2018). The population having mostly poor income earners, generally use medicinal plants, such as *P. guineense* and *Xylopia aethiopica*, to cure and treat various types of diseases. Due to its numerous medicinal plants, the area is a good source of a diversity of bioactive compounds, which could serve potential lead compounds for drug discovery (Olorunnisola et al. 2013; Ehimemen and Salisu 2020).

The World Health Organization (WHO) observations show that many African and developing counties utilize these medicinal plants to cure infectious diseases. The populations often patronize traditional medicine practitioners (TMPs) and herb vendors for their principal healthcare needs. These TMPs collect medicinal plants easily accessible from the forests or from their farms to prepare decoctions and several herbal formulations to treat diseases. Medicinal plants growing in tropical rainforest zone are rich sources of bioactive compounds and as such the ethnobotanical information of such plants are required for active use as an antimicrobial lead compounds (Abou-Kassem et al. 2021; El-Saadony et al. 2021f; Saad et al. 2021). In West Africa, the significance of traditional medicine cannot be overemphasized because of the lack of modern facilities in the rural areas (Ode et al. 2011).

Traditional and medicinal uses of *P. guineense*

P. guineense is useful in conventional medicine, and its nutritive and medicinal potentials have been outlined in several pharmaceutical studies (Obodozie et al. 2010; Uhegbu et al. 2015; Ene-Obong et al. 2018). The fruits, seeds, and leaves are often prepared with alcohol or as decoctions together with other herbal formulations and used in treating various diseases (Freiesleben et al. 2015; Besong et al. 2016; Isikhuemen et al. 2020). Ethno-pharmacologically, the roots, leaves, fruits, and seeds of *P. guineense* are relevant herbal products in African traditional medicine, most importantly in West Africa. It is administered to nursing mothers to stimulate breast milk production and support the contraction of the uterus after childbirth (Okigbo and Igwe 2007).

The fruits and seed extracts from this plant are essential ingredients in the preparation of niprisan herbal formulation, which is successfully employed in treating of sickle-cell anemia (Obodozie et al. 2010; Freiesleben et al. 2015; Amadi et al. 2019). Decoctions from young seeds and fruits have been used to save individuals from venereal infections, rheumatism, gastrointestinal tract disorders, and respiratory tract infections (Udoh 1999). *P. guineense* extracts are used to treat mental disorders, and fever. It was also found to possess sedative and muscle relaxant properties (Oyemitan et al. 2015).

Extracts from *P. guineense* are used as aphrodisiac, and it has been reported that Yaji soup, which is eaten

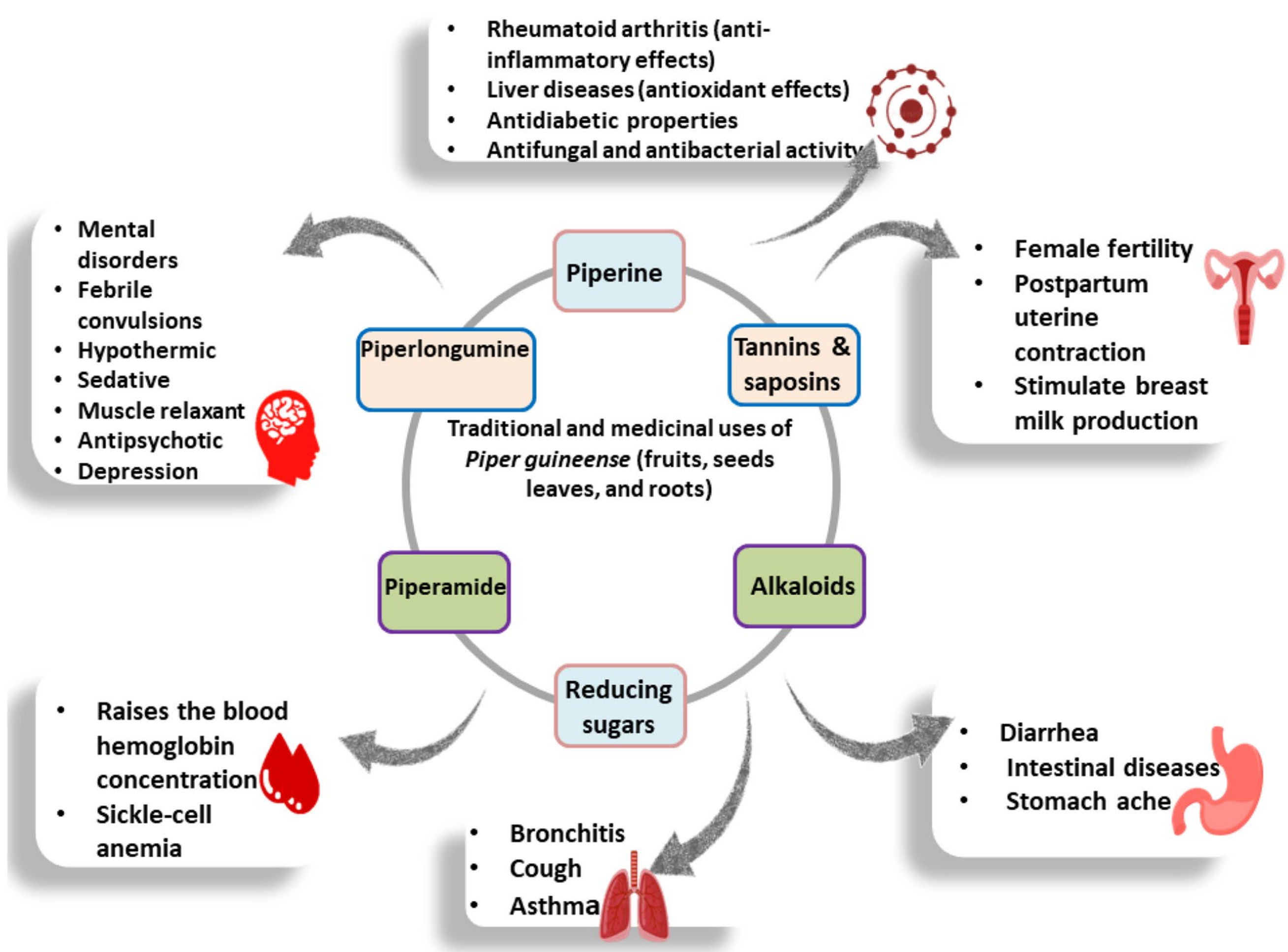

Fig. 3 Traditional and medicinal uses of black pepper (*Piper guineense*)

as an aphrodisiac in most West African countries, is prepared from the fruits of *P. guineense* (Ibrahim et al. 2010; Asase et al. 2012). Infusions and decoctions from the fruits of *P. guineense* are administered orally to treat bronchitis, cough, and intestinal diseases (Nwozo et al. 2017; Kambiré et al. 2019). Several studies have shown that extracts of *P. guineense* could lower lipid peroxidation, thereby preventing inflammation and oxidative damage, and are also used to treat dysentery (Ogunniran 2009; Nwozo et al. 2017; Isikhuemen et al. 2020). The leaves, fruits, and whole plant parts of *P. guineense* are used to prepare herbal formulation for the treatment of asthma and its related symptoms (Gbekley et al. 2017). Previous research conducted on the ethnomedicinal uses of African medicinal plants has reported that the leave extracts of *P. guineense* are used to treat sexually transmitted diseases (Ajibesin et al. 2011; Amadi et al. 2019).

The fruits and leaves of *P. guineense* are ground and soaked in alcohol with other herbs to prepare concoctions used tor the treat epilepsy, convulsion, and malaria (Abila et al. 1993; Umoh et al. 2013). Previous research has shown that *P. guineense* extracts are helpful in treating fertility disorders (Mbongue et al. 2005). It has been used to stimulate sexual behavior in an adult male rat (Kamtchouing et al. 2002). It is also used as a food preservative and fragrance in the perfume and cosmetic industries (Nwozo et al. 2017). Traditional and medicinal uses of *P. guineense* are summarized in Fig. 3.

Antibacterial activities of *P. guineense*

P. guineense is an African medicinal plant used by traditional healers for various medicinal purposes and more often as herbal remedies for treating symptoms related to bacterial infections, such as diarrhea, cough, and rashes. Bacterial infections often result in death if not well treated, and *P. guineense* has been widely reported to exhibit antibacterial properties (Okeke et al. 2001; Konning et al. 2004; Anyanwu and Nwosu 2014).

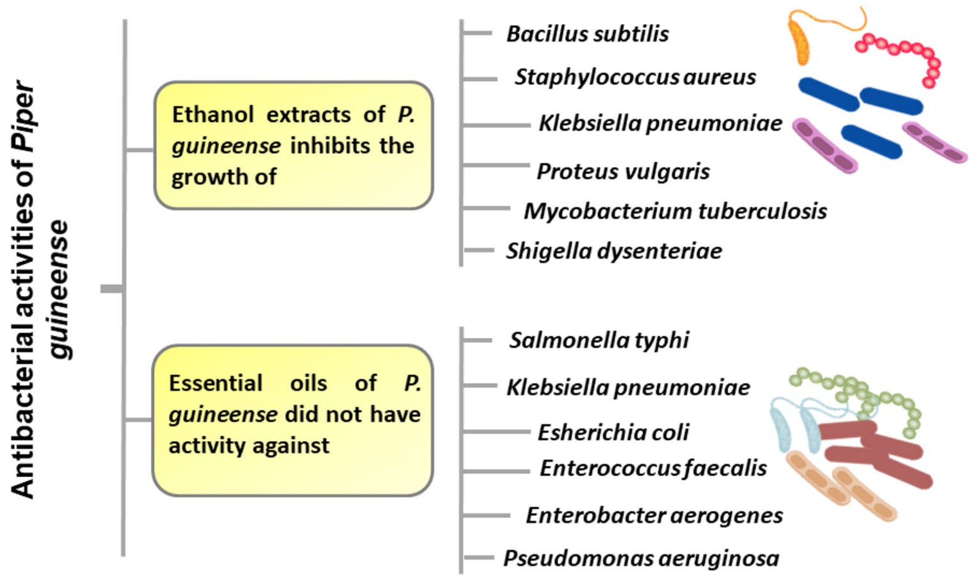

Fig. 4 The antibacterial activities of black pepper (*Piper guineense*)

Extracts and fractions from various parts of this plant have antibacterial activity against Gram-positive and Gram-negative bacterial strains (Tekwu et al. 2012; Dada et al. 2013; Amadi et al. 2019). It has been observed that the extraction solvent and method of extraction affect the inhibitory activity of the extracts on bacteria. Previous research has shown that hexane, methanol, and ethanol extracts are more effective than the water fractions (Konning et al. 2004; Dada et al. 2013). However, essential oils from the fruits of *P. guineense* did not have any activity against *E. coli*, *Salmonella typhi*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* (Olonisakin et al. 2006). *P. guineense* is effective against *M. tuberculosis*, which is a threat to human life (Tekwu et al. 2012).

The ethanol extracts of *P. guineense* have been reported to be effective against *B. subtilis*, *E. coli*, *S. aureus*, *S. typhi*, *K. pneumoniae*, and *Proteus vulgaris* (Okeke et al. 2001). The antibacterial evaluation of the plant extracts on *E. faecalis* did not exhibit remarkable activity (Okigbo and Igwe 2007; Amadi et al. 2019). The antibacterial activities of *P. guineense* on *Acinetobacter* spp., *B. cereus*, *E. coli*, *Salmonella* spp., *Shigella dysenteriae*, and *S. aureus* (Dada et al. 2013; Kambiré et al. 2019) revealed that the bioactive compounds from *P. guineense* are good antibacterial agents and could be a lead to the discovery of new antibacterial drugs.

Previous research has shown that ethanol extracts from *P. guineense* possess remarkable activity against *E. coli* (Anyanwu and Nwosu 2014). These researchers observed that the extracts inhibited the growth of *B. subtilis*, *E. coli*, *S. aureus*, and *P. aeruginosa* (Anyanwu and Nwosu 2014). The bacterium causes urinary tract and lower respiratory tract infections. *P. guineense* extracts were very effective against *P. aeruginosa* (Lister et al. 2009; Rasamiravaka et al. 2015).

Other extracts of the fruit of *P. guineense* also exhibited promising inhibitory activity against *Enterobacter aerogenes*. Previous research showed that the plant-derived compounds and plant extracts could be potential sources for new antibacterial drugs against multi-drug-resistant bacteria (Subramani et al. 2017).

P. guineense could be explored as a lead to new antibacterial drugs to treat human infections (Lam-Himlin et al. 2011; De Meij et al. 2017). The antibacterial activities of *P. guineense* are summarized in Fig. 4.

Antifungal activities of *P. guineense*

Various reports indicate that *P. guineense* extracts potentially inhibit the growth and propagation of fungal infections such as vaginosis, skin rashes, and oral thrush. This herb may behave as a modern antifungal scaffold in Africa, while its fruits and leaves are the best plant parts for treatments (Mgbeahuruike et al. 2019).

Additionally, this traditional healer is successfully used instead of many other costly conventional antifungal agents (Abiala et al. 2015; Mgbeahuruike et al. 2019). Piperlongumine and piperine were found to be effective against *C. albicans* with a minimum inhibitory concentration of 39 and 78 μg/mL, respectively (Mgbeahuruike et al. 2019).

C. albicans is a dimorphic opportunistic pathogenic yeast which cause serious fungal diseases in humans particularly the patients suffering from acquired immunodeficiency syndrome (Brown et al. 2014). *P. guineense* extracts were found to be very effective against *C. albicans*. Further advocating the potential of *P. guineense* as an antifungal agents, results revealed that the leaf and fruit extracts of *P. guineense* inhibited the growth of various *Candida* strains (i.e., *C. albicans*,

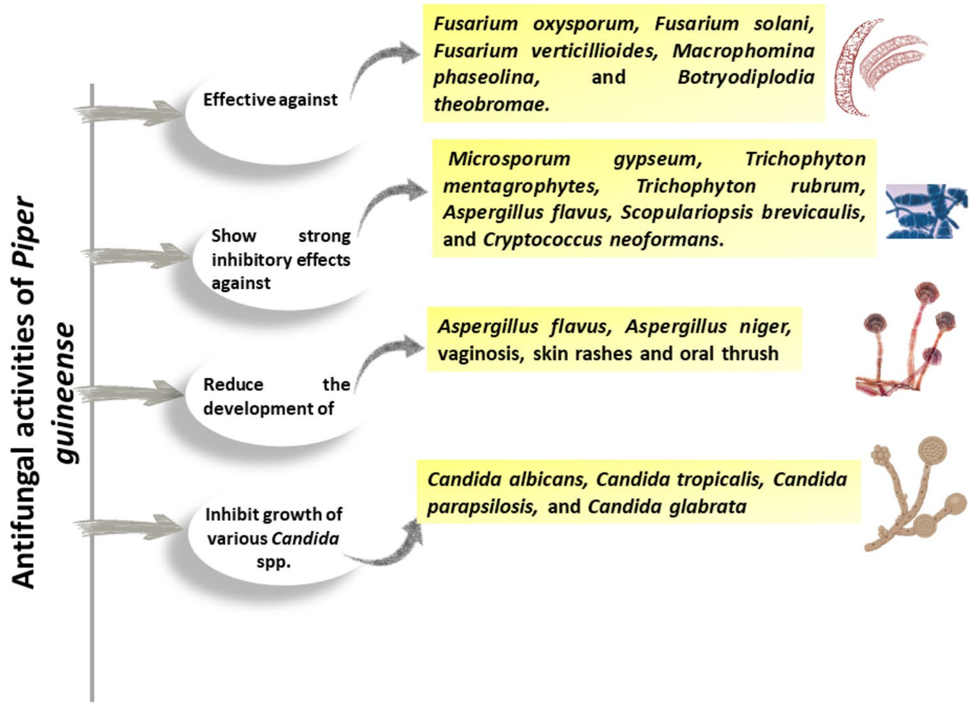

Fig. 5 The antifungal activities of black pepper (*Piper guineense*)

C. tropicalis, *C. parapsilosis*, and *C. glabrata*), thus defining its usage in the treatment of sexually transmitted diseases (Brown et al. 2014). *P. guineense* also showed strong inhibitory effects against human infections caused by the filamentous fungi, i.e., *Microsporum gypseum*, *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Aspergillus flavus*, *Scopulariopsis brevicaulis*, and the yeast *Cryptococcus neoformans*.

Extracts, essential fractions, and natural products derived from *P. guineense* also have the ability to save skin from various fungal infections (Ngane et al. 2003; Imo et al. 2018). Furthermore, *P. guineense* have reduced the development of *A. flavus* and *Aspergillus niger* (Dada et al. 2013).

P. guineense was also found to be effective against many fungal plant pathogens (i.e., *Fusarium oxysporum*, *Fusarium solani*, *Fusarium verticillioides*, *Macrophomina phaseolina*, and *Botryodiplodia theobromae*), which is a primary reason for causing rots in vegetable and watermelon fruits (Abiala et al. 2015). Extracts of *P. guineense* have the ability to improve the shelf-life of carrots and potatoes (Amaeze et al. 2013).

Antifungal property of extracts of *P. guineense* might be associated with its alkaloid compounds. Moreover, piperyline and 4,5-dihydropiperylin, which are present in the hexane fraction of *P. arboretum* exhibited antifungal activity against *C. parapsilosis*, *C. neoformans*, and *C. krusei* (Regasini et al. 2009).

Extracts derived from the leaf of medicinal plants have high affinity to control pathogens compared to the extracts derived from other parts of the plant (Rahmatullah et al. 2012). Oral ingestion is the preferred way of drug administration. Herbal medicines are the cornerstone of traditional healers. The decoctions derived from the leaves and fruits, prepared in mild alcohol, have been found effective when administrated orally to control fungal infections, such as *Candida* vaginosis or thrush on the tongue (Maroyi 2013). The antifungal activities of *P. guineense* are summarized in Fig. 5.

Amides and alkaloids in *P. guineense*

Novel amides and alkaloids from roots of *Piper* species, including *P. guineense*, are known as piperamide extracts. This piperamide possesses well-defined antibacterial, antifungal, anti-inflammatory, and anticancer properties. Hence, these piper species are gaining popularity globally, but particularly in Africa as a folk medicine and paving the way for modern drug inventions (Bezerra et al. 2005; Nageswari et al. 2018).

Piperine is a naturally occurring amide alkaloid with potent antimicrobial properties, mainly extracted from the *P. guineense* (Adesina et al. 2003; Scott et al. 2005). *P. guineense* also contains other peak piperamide alkaloids such as 4,5-dihyropiperlonguminin, piperlonguminin, 4,5-dihydropiperine, and piperylin (Scott et al. 2005).

Conclusion

P. guineense extracts used for various medicinal purposes and as herbal remedies may lead to possible development of new antimicrobial drugs. Alkaloids are the primary biologically bioactive compounds significantly present in *P. guineense* extracts. The water extracts were devoid of these alkaloids, hence, inactive against most of the studied bacteria and fungi. This review discussed the efficacy of *P. guineense*, as a strong antibacterial and antifungal agent against a broad panel of Gram-positive and Gram-negative bacteria, as well as a large set of fungal strains, including important human pathogens. *P. guineense* possess many effective sources of piperamide compounds that can be used to inhibit bacterial and fungal infections. Further studies could be conducted to evaluate the piperamide compound mechanism as an antibacterial and antifungal drug. Moreover, it is of importance to highlight the piperamide compounds for their anti-biofilm property, including quorum sensing. The inhibitory activity recorded with the various fractions and extracts against the evaluated bacterial and fungal strains needs further research on the bioactive compounds from *P. guineense*. Furthermore, studies could also be focused on evaluating *P. guineense* extracts in combination with *Xylopia aethiopica* and other medicinal plants for their antibacterial and antifungal effects. For these investigations, herbal formulations identical to those used to treat infectious diseases by traditional healers in African traditional medicine could be used.

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Declarations

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