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Antimicrobial and antihelminthic impacts of black cumin, pawpaw and mustard seeds in livestock production and health

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Abstract The resistance of microbial strain to the use of medically important antibiotics, high cost of production, and the resistance of ecto and endoparasite to anthelminthic and acaricidal is a cause for concern. There has been intensified effort in search for alter-natives to synthetic drugs. Such alternative must be able to kill, reduce, or inhibit pathogenic microbial population while improving the commensal microbes’. Black cumin (Nigella sativa Linn.), paw-paw (Carica papaya Linn.) and mustard (Brassica nigra Linn.) seeds fit into those categories. The antimicrobial functions of black seeds, is preventing

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the formation of biofilm among microbial strain. The glucosinolate compound in it could be degraded in

1. h by incubating it with fungi (Aspergillus sp. NR-4201) strain. Similarly, Enterobacter cloacae is capable of degrading benzyl isothiocyanate content of mustard. The 15% inclusion of mustard oil in vitro was capable of reducing methane formation. Sinapine a derivative of mustard is cable of enhancing the growth of some microbes except Escherichia coli and thus a potential probiotics. Pawpaw seed is very potent in their control of wide range of ecto and endo parasites. However, seeds of black cumin, pawpaw and mustard might be incorporated into livestock nutrition.

Keywords Allyl isothiocyanate Benzyl isothiocyanate Livestock Thymoquinone Tropical plants

Introduction

Livestock and crop production have been independent on one another from the start of animal existence; this is evident in the ability of animal in the wild to self-medicate when ill. However, a new relationship between crop and livestock as regards animal health rather than animal nutrition is not novel but seems to be an interesting development. This relationship is

123



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embedded on the phytochemicals or bioactive com-ponent in plants which are of health benefit to livestock if harnessed and used in right quantity. Bioactive components from plants have been a source of health for animals in the wild and medicine for survival of humanity. Usually, animals in the wild and other scavenging animals self-mediate by consuming plants which contain some medicinal properties. Due to intensification, which led to increased morbidity and mortality in animals, farmers started using antibi-otics and vaccines against disease causing organisms.

However, improper dosage, non-adherence to with-drawal period, and continual use of antibiotics led to the development of resistance among microbes. However, they became non-responsive, because they are now ‘familiar’’ with such antibiotics. This devel-opment necessitated the need to ban the use of antibiotics in livestock production at sub-therapeutic level and the recommended ban on the use of any medically important/high priority antibiotics by world health organization. Implementing alternative feeding strategies is imperative in modern animal nutrition, especially in young animals that are most sensitive to health disorders (Windisch [2009](#page15)). In order to find solution to this challenge, there might be need for us to revert back to the means by which animals survive in the wild without the use of synthetic antibiotics.

Studies have shown through the development of some medicines used by humans that plant contains bioactive compounds that are capable of promoting good health through its antimicrobial, anti-parasitic, hematological and other important health parameters. A potential plant should be able to kill, reduce, or inhibit pathogenic microbial population while improv-ing the commensal microbes. Exploring the options of mustard, black cumin and pawpaw seeds might also be part of those plants capable of functioning as phyto-genic feed additives. The essence of this review is to evaluate the nutraceutical, antimicrobial activity and mode of action of black cumin, mustard, and pawpaw seeds.

Seeds phytochemical content in black cumin, mustard and pawpaw seeds

Generally, plants and their products contain flavonoid, saponin, alkaloid, tannin, polyphenol and they exert different benefits and functions in animal. Some

functions as antimicrobial, antioxidant, and detoxifier. Large number of simple phenols and phenolic acids possess antimicrobial activities against wide range of gram positive and negative microbes but at varying concentrations (Patra [2012](#page14)). This antimicrobial activ-ity is due to the bioactive compounds accumulated in plant tissues (Pavarini et al. [2012](#page14)). Polyphenols are antioxidant designed by nature to prevent oxidation of lipid or oil derivatives from different plant part especially those in embedded in plant seeds. Phenolic compounds play various physiological one of which is protecting plants against fungi, bacteria and viruses (Cartea et al. [2010](#page12)) some of which are disease causing organisms.

Black cumin seeds (Nigella sativa Linn.)

The N. sativa Linn. has many bioactive ingredients of which thymoquinone present up to (30–48%) is the most abundant, amongst others such as flavonoids, anthocyanins and alkaloids (Ahmad et al. [2013](#page12); Desai et al. [2015](#page12)). Furthermore, black seeds also contain Other authors identified thymoquinone containing up to 50% as the main component besides, p-cymene (40%), pinene (up to 15%), dithymoquinone, thymol and thymohydroquinone (Lutterodt et al. [2010](#page13)), terpene derivatives-limonene, carvacrol alpha-pinene, 4-terpineol, longifolene, and t-anethole benzene (Gharby et al. [2015](#page13); Goel and Mishra [2018](#page13)), 2-methyl-4-isopropyl-p-quinones, anthraquinones, glycosides, melanthin (Akhtar [1988](#page12)), nigellone, beta-sitosterol, flavonoids, that could have positive impact on human and animal health (Paarakh [2010](#page14); Javed et al. [2012](#page13)). Three flavonoids namely quercetin and kaempferol 3-glucosyl and quercitin are present in black seeds (Merfort et al. [1997](#page14)) while saponins (Alpha-Hedrin, Steryl-glucosides and acetyl-steryl-glucoside) (Ansari et al. [1988](#page12); Kumara and Huat [2001](#page13)) are present in black seeds. Sharma et al. ([2009](#page14)) reported the alkaloids in black cumin seeds belongs isochinoline alkaloids (nigellimin and nigellimin-N-oxide) and pyrazol alkaloids (nigellidin, alphahederin and nigellicin) (Khan [1999](#page13)) (Fig. [1](#page4)).

Mustard seeds (Brassica nigra Linn.)

The mustard plant contains organo-Sulphur compound known as glucosinolates. The hydrolysis of this compound by myrosinase (thio-glucoside hydrolases,

123

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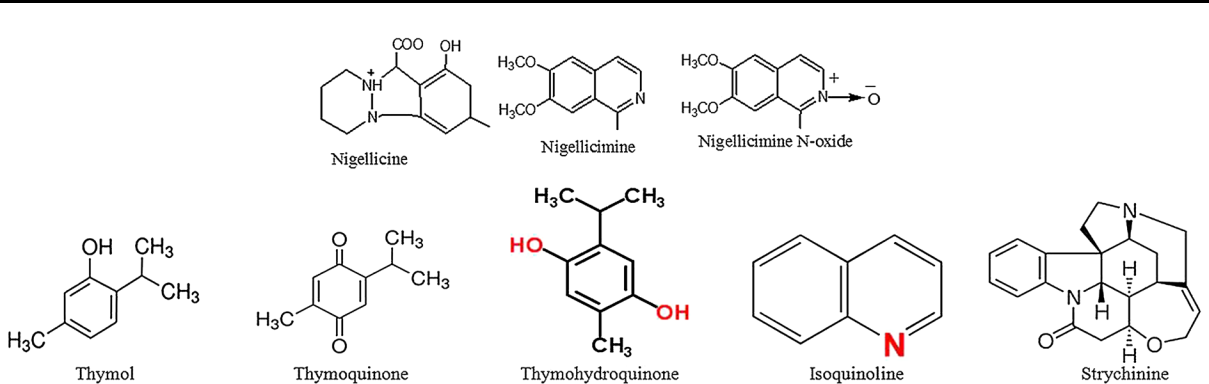


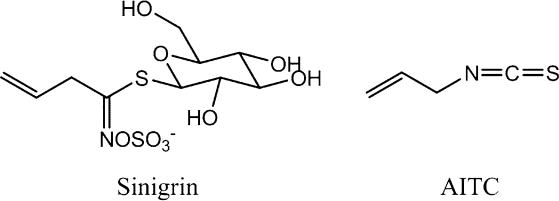
Fig. 1 Structures of the chemical constituent of black cumin seed (Yessuf [2015](#page15))

EC 3.2.3.1) enzyme produces allyl isothiocyanate known to be responsible for the pungent/stringent taste of mustard; and sometimes the glucosinolates are hydrolysed by gut microbes (Abul-Fadl et al. [2011](#page12)). Sinigrin is the main glucosinate found in mustard alongside other component such as sinalbin and glucobrassicin (Abul-Fadl et al. [2011](#page12)). Isothio-cyanates are present in about 0.8–2.3% (Cui and Eskin [1998](#page12)) with allyl isothiocyanate approximately 1% depending on the breed of mustard (Polat [2010](#page14)). After enzymatic hydrolysis, Allyl (also known as sinigrin) and 3-butenyl (also known as gluconapin) glucosinolate are in brown mustard which are volatile, while sinalbin produces nonvolatile p-hydroxybenzyl glucosinolate in found in white mustard (Fahey et al. [2001](#page13); Abul-Fadl et al. [2011](#page12)). Black mustard (Brassica nigra) contains tannins, alkaloids, and flavonoids (Obi et al. [2009](#page14)) and other minor component such as phytin (Fahmi [2016](#page13)). Furthermore, mustard seeds contain Vanillin 2.57 mg/kg, Sinigrin 0.7 mg/kg, Catechin 0.06 mg/kg, Quercetin 0.13 mg/kg. Sinigrin repre-sents about 97.1% of the glucosinolate concentration (Parikh and Khanna [2014](#page14)) while it is present on the average in about 98.5% of mature mustard leaves (Frazie et al. [2017](#page13)). Sinigrin being a precursor of allyl isothiocyanate shows that efficient use of mustard leaf might serve as important antimicrobial options in livestock production (Fig. [2](#page4)).

Pawpaw seeds (Carica papaya Linn.)

The papaya seeds contain carpaine, caricin, glu-cotropaeolin, benzyl glucosinolates, benzyl isothio-cyanate, benzyl thiourea, hentriacontane, and b-sitosterol (Kumar and Devi [2017](#page13)). Similarly, papaya

Fig. 2 Chemical structure of mustard component (Sporsheim et al. [2015](#page14))



seed contains total phenol 131 mg gallic acid equiv-alent/100 g, total flavonoid (191.06 mg Quercetin equivalent/100 g) (Dada et al. [2016](#page12)) and 30.32 total phenol (Maisarah et al. [2014](#page13)). Glucosinolates, cyano-genic glucosides, and saponin glycosides are passive compounds and are less toxic while they remain intact in plant vacuole (Osbourn [1996](#page14)). However, if cell wall integrity is compromised by damaging (due to human activity and animal activity) or microbes, glycoside or glucosinolates are hydrolysed by myrosinase present in the separate part of the plant cell; to release toxic aglycone (Osbourn [1996](#page14)) (Fig. [3](#page5)).

Antimicrobial activity of black cumin, mustard and pawpaw seeds

Nutritional manipulation of commensal gut microbes as a means of enhancing intestinal functions is an interesting approach to prevent disease in animal and human (Sahoo and Soren [2012](#page14)). Gut microbes influ-ence nutritional, immunity system, economic, health, endocrine system of livestock and the health of consumers. Nutritional quality of animal food product and the properties of animal wastes are influence by the extent of microbes residing in the gut (Patra [2012](#page14)).

123

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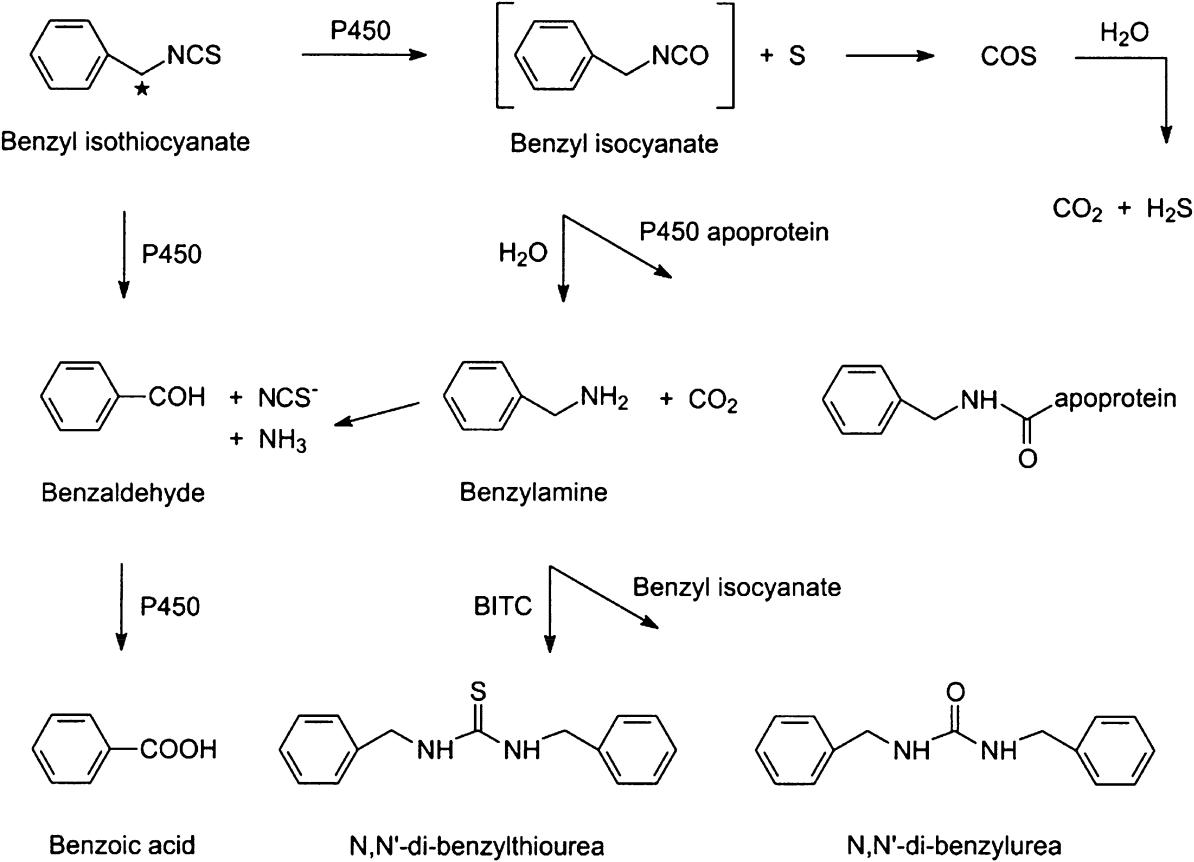


Fig. 3 Structures of some chemicals in pawpaw seed (Goosen et al. [2001](#page13))

The use of antibiotics in treatment and prevention of diseases often has a negative effect on host tissues and organ (Lohidas et al. [2015](#page13)). To protect animals from tissue and organ damage, use of plant and plant extract due to the bioactive compound present are highly recommended due to their potential. Several microbes residing in the gut are food borne disease and reducing their population in the gut might prevent or reduce the instance of food borne disease. For instance, E. coli, Campylobacter jejuni, Salmonella sp., Listeria mono-cytogenes and indirectly protecting the animal itself from the proliferation of pathogenic microbes such as coccidia parasite, and C. perfringens. Studies have shown the antimicrobial activity of plants against disease causing microbes such as E. coli and C. perfringens, which help to reduce the development of secondary problem like colibacillosis and necrotic enteritis (Jamroz and Kamel [2002](#page13); Mitsch et al. [2004](#page14)).

Black cumin seeds (Nigella sativa Linn.)

Black cumin seed contains many bioactive com-pounds that is common among other plants such as flavonoid, polyphenol, saponin etc. uniquely, black cumin seed contains thymoquinone which a wide range of anitmicorbial activity against gram positive and gram negative bacteria. El-Nagerabia et al. ([2012](#page12)) evaluated the effect of black cumin oil (1, 2 and 3 ml/ 100 ml) on growth and production of aflatoxin B1 by Aspergillus parasiticus (CBS 921.7) and Aspergillus flavus (SQU 21) strains. One and 2 ml/100 ml of N. sativa Linn. oil was able to inhibit aflatoxin B1 by 49.7–58.3% while 3 ml/100 ml inhibited aflatoxin production by 32–48% but they had no effect Aspergillus species. This inhibition effect could be that N. sativa Linn. seed oil transpired with the biosynthesis pathway of aflatoxin (El-Nagerabia et al. [2012](#page12)).

123

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Khan et al. ([2012](#page13)) evaluated different levels (0, 2.5%, and 5%) of black cumin seeds and 0.1% antibiotics on ceacal microbial population of broilers. The influence of black cumin seeds on pathogenic microbes like coliforms and E. coli at 2.5% and 5.0% supplementation was similar to the antibiotics used. This reduction in pathogenic microbes would help to decrease the competition for nutrient with beneficial commensal microbes. Although E. coli is a commen-sal microbes of the gut, excessive proliferation might increase that concentration of lipopolysaccharide (endotoxins) which might enter the blood stream through inflammation of the gut hence reducing the function of the tight junction of the enterocytes to damage the liver and reduce growth rate and giving room for secondary infections and indication of weakened immune system. So by inhibiting their growth, there won’t be need for them to be killed let alone have overwhelming level of lipopolysaccha-ride; as endotoxin consist of 75% of gram negative cell walls (Biomin [2016](#page12)) Microbiota shifts affect mor-phology of the gut wall and induce immune reactions, which by affecting energy expenses of the host animal may promote their growth (Teirlynck et al. [2009](#page15)).

Similarly, Abd El-Hack et al. ([2018](#page12)) evaluated the antimicrobial activity of cold-pressed black cumin oil in quail for 6 weeks. The black cumin oil was supplemented at (0, 0.5, and 1.0 g/kg diet). The black cumin oil reduced ileal population of total bacterial count, coliform, E. coli, and Salmonella sp. more than the control while 1.0 g/kg black cumin oil was lower than 0.5 g/kg. The reason for this might be attributed to the synergy of phytochemicals (thymoquinone, Flavonoids etc.) present in black cumin oil.

Mustard seeds (Brassica juncea Linn.)

Mustard seed is rich in bioactive substances such as glucosinolates and phenol compounds. Sinigrin and sinalbin are two major glucosinolates found in oriental and yellow mustards, respectively (Herzallah and Holley [2012](#page13)) allyl isothiocyanate and benzyl isothio-cyanate are the main hydrolysis by-products derived from sinigrin and sinalbin, respectively (Herzallah and Holley [2012](#page13)). Antimicrobial activity of mustard bioactive compound may be classified as phenolic (sinapic) and non-phenolic (allyl isothiocyanate). Antimicrobial properties of extracts from brown mustard (Brassica juncea Linn.) and yellow (Sinapis

alba L.) mustard seeds have been attributed to their glucosinolates and isothiocyanates content (Fahmi [2016](#page13)).

Many microbes in animal product are acquired form the gut of animals during processing. In Nigeria, Salihu et al. ([2009](#page14)) reported the high prevalence of thermotolerant Campylobacter species in chicken with Campylobacter jejuni [ Campylobacter coli [ Campylobacter lari. This occurs as a result of contamination between gut microbes and meat during processing. This high incidence of thermotol-erant Campylobacter species is a cause for concern especially in developing countries with poor medical facilities. Its ability to survive in high temperature could mean that they might not be completely eliminated during scalding or boiling. Thus reducing the population of food borne microbes might go a long way in reducing food borne morbidity and mortality in consumers. Sinapic acid against various Gram-negative and Gram-positive (Engels et al. [2012](#page13)). Gut microbial population dynamics may be influenced by the ability of phenolics to suppress or stimulate some certain members of the microbial community (Tzounis et al. [2008](#page15)). In another study (Fahmi [2016](#page13)) phenolic derivatives (sinapic and sinapine) of mustards were tested against strains of Escherichia coli O157:H7 (02:0304, 02:0627, 02:0628, 00:3581, 02:1840) and Listeria monocyto-gens (2-243, GLM3, GLM4) for their antimicrobial ability. The sinapic acid was reducing the microbial

growth with increasing concentration (0.58–3000 ppm). In contrast, sinapine acid

(0.52–1071 ppm) increased the growth of the Escherichia coli and Listeria monocytogenes. The growth started increasing at between 16.73 and 1071 ppm. Cueva et al. ([2010](#page12)) reported that antimi-crobial activity of phenolic acids against gram-negative bacteria depends on the stain of the microbe considered. Escherichia coli O157:H7 (02:1840) strain was the only microbe whose growth decreased with increasing Sinapine. The effect on this particular strain could be genetically in that the peptidoglycan of this strain is weaker compared to other strain hence allowing easy permeability of the sinapine into the cell organelles thus inhibiting the growth. The inhibitory activity of sinapic acid (2.2 mM) against Escherichia coli was attributed to the presence of methoxy and two hydroxyl groups on the benzene ring of sinapic acid (Tesaki et al. [1998](#page15)). The

123

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conversion of sinapic acid in plant extracts to sinapine seems to be important for the antibacterial activity. However, the selective stimulation of the growth of beneficial commensal bacteria species and strains by sinapine which is a product of mustard extract could be developed into prebiotic products (Fahmi [2016](#page13)).

Enterobacter cloacae strains are capable of degrad-ing benzyl isothiocyanate into benzylamine and hydrogen sulfide (Tang et al. [1972](#page15)). Kakimoto and Armstrong ([1962](#page13)) also found p-hydroxybenzylamine in the urine of human subjects who had ingested mustard previously. The detection of p-hydroxyben-zylamine in white mustard (Larsen [1965](#page13)), a rich source of p-hydroxybenzylglucosinolate.

Pawpaw seeds (Carica papaya Linn.)

Glucotropaeolin is the precursor to benzyl isothio-cyanate (Peterson [1970](#page14)). The benzyl isothiocyanate is a bioactive substance present in the papaya seed that has been studied among different areas due to its wide applications (Barroso et al. [2016](#page12)). In Peter et al. ([2014](#page14)) 25, 50, 75, 100 mg/ml concentration of methanol and aqueous extract of papaya seed was tested for their antimicrobial properties against Staphylococcus aur-eus, Pseudomonas aeruginosa, and Escherichia coli. Inhibition increased with increasing concentration of pawpaw seeds. Furthermore, methanol extract was more effective than aqueous extract. This implies that methanol was able to extract more active component form pawpaw seeds than water.

Antimicrobial action of seeds phytochemicals

Although wide range of phytochemicals are weak molecules and are narrow-spectrum in their activities, they can act on multiple biochemical targets (Simo˜es et al. [2012](#page14)). The mode of action of these substances originates from the stabilization of gastrointestinal functionality during episodes of adverse hygienic conditions (Windisch [2009](#page15)). Moiety structure, chain length and sugar composition affect antimicrobial activity of saponin (Patra [2012](#page14)). Thus, there is a degree of relationship between the structure of saponin and antimicrobial activity (Patra [2012](#page14)) which is positive. Saponins are reported to perform its antimi-crobial activity by being toxic to cell through

compromising the integrity of cell membrane to increase permeability (Okigbo et al. [2009](#page14); Coleman et al. [2010](#page12); Augustin et al. [2011](#page12)). The permeability of the cell membrane by saponin might be caused by, triterpenoid moiety which binds to the lipid sterol in cell membrane (Sampedro and Valdivia [2014](#page14)). This sugar moiety could force the cell membrane to curve due higher concentration of saponin leading to pore formation or disrupted lipid raft (Sampedro and Valdivia [2014](#page14)). The pore formation causes cell shock as a result of changes in cell pH and flow gradient which result in cell organelles shrinkage and cytosol content to leaks or drain out to the environment by osmosis which eventually causes cell plasmolysis. Glycoside saponins could structure that looks like pore which modify cell wall permeability resulting in altered ion balance between intracellular and extra-cellular biosystem (Melzig et al. [2001](#page13)). Interference with cell energy metabolism via interaction with catabolic enzymes and the electron transport chain (Mandal et al. [2005](#page13); Sinha Babu et al. [1997](#page14)) is also possible.

Antimicrobial activity of tannin has been attributed potentially to their ability directly damaging it cell membrane, by reacting with proteins that are soluble but stable in water or bind to cell polysaccharides or enhance enzymes inactivation (Cowan [1999](#page12)). One of the secondary metabolites that are abundant in nature (plant species) is flavonoids (Patra [2012](#page14)). The free radical scavenging potency of flavonoids has been attributed to their antibacterial activity (Yamato and Gayor [2002](#page15)). Antimicrobial activity of flavonoid might be through compromise of cytoplasmic mem-brane, inhibition of DNA gyrase, dehydratase of b-hydroxyacyl-acyl protein carrier (Cushnie and Lamb [2005](#page12); Zhang et al. [2008](#page15)), and interference with quorum sensing mechanism to inhibit the disease causing ability/virulence of bacteria (Vandeputte et al. [2011](#page15); Cushnie and Lamb [2011](#page12)). Dietary flavonoids are transformed by microbes in the intestine to potent antimicrobial compounds (Patra [2012](#page14)).

The length of alkyl chain determines the antimi-crobial effect of phenolic acid (Merkl et al. [2010](#page14)). The toxicity of phenolic acid to microbes is determined by the existence of hydroxyl group and oxidative activity of phenol (Patra [2012](#page14)). Increasing hydrophobic alkyl chains could disrupt the fluidity of cell membrane. The phenolic acids could enter the molecular structure of the membrane with the polar hydroxyl group oriented

123

Agroforest Syst

into the aqueous phase by hydrogen bonding and nonpolar carbon chain aligned into the lipid phase by dispersion forces (Kubo et al. [1995](#page13)) reported that phenols and phenolic acids can cause enzyme inhibi-tion by oxidizing products which disrupt energy production through more nonspecific interfaces with the proteins (Mason and Wasserman [1987](#page13)). However, it might be attributed to their ability to penetrate the organism cell membrane and inactivating functional enzymes compromising the cellular integrity and leading to dysfunctional cell and death due to the hydrophobicity of phenolic compounds (Cetin-Karaca [2011](#page12); Moreno et al. [2006](#page14)).

Plant peptides carry out their antibacterial activity by forming ion channels in the cell membrane and preventing bond of microbial proteins to host polysac-charide receptors (Suarez et al. [2005](#page14); Zhang and Lewis [1997](#page15)). The antimicrobial mode of action of hydrophobic essential oil is their ability to interfere with bacterial cell membrane, degenerate structures of the membrane and causing leakage of ions which is enhanced by their lipophilic nature making it easier to enter cell membrane (Windisch et al. [2008](#page15)). The antimicrobial activity of terpenes which are in abun-dance in essential oil is promotion of membrane disruption while coumarins cause reduction in cell respiration which is the means by which energy is produces in the mitochondrion. This reduced or inhibited energy production would eventually kill the cell (Ya et al. [1988](#page15)).

Thymoquinone of black cumin seeds

Biofilm formation is the means by which microbes reduce the impact of antibiotic; by hiding themselves within the polymeric matrix (Høiby et al. [2010](#page13)). Chaieb et al. ([2011](#page12)) reported thymoquinone which is a bioactive ingredient helps to prevent biofilm forma-tion among bacteria. This is very advantageous to in livestock production as biofilm is usually the protec-tive screen used by pathogenic microbes to protect themselves from the impact of antibiotics or chemical that could destroy them; allows microbes to survive in hostile environmental conditions (Mah and O’Toole [2001](#page13)). This could also mean that by combining black cumin seeds with other plant part or bioactive ingredient more potent than thymoquinone, it could lead to a synergy of bioactive ingredients. As

thymoquinone would be preventing biofilm formation, other active ingredients would be inhibiting, lysing, blebbing or denting the microbes.

In Goel and Mishra ([2018](#page13)), thymoquinone per-formed it antimicrobial function by dents and bleb-bing, cell lysis and prevention of biofilm formation and was capable of destroy biofilm forming between 6 and 24 h, but does not show cell membrane damaging characteristics. 12.5 lg/ml of thymoquinone was required for to prevent Bacillus subtilis and Pseu-domonas aeruginosa, 50 lg/ml for Staphylococcus aureus and 250 lg/ml for Escherichia coli to prevent more 90% biofilm.

Another mechanism of action of Thymoquinone is through generation of ROS which impaired cellular electron transport, leading to prolonged oxidative stress which causing irreversible damage to bacterial DNA, proteins, and membrane leading to cell death due to quick aging (Martinovich et al. [2016](#page13); Goel and Mishra [2018](#page13)). Thymoquinone are bifunctional because they can protect the cell from oxidative stress, and can also induce stress in cells. The former is by intracellular reduction by (quinone oxidoreductase 1) of thymoquinone to dihydrothymoquinone with the reduced compound scavenging for free radicals, including hydroxyl radical, singlet oxygen, superoxide anion radical (Nagi and Mansour [2000](#page14)) or by coun-tering xanthine oxidase system in order to obstruct generation of oxidative stress (Badary et al. [2003](#page12)). While the latter is by reduction of thymoquinone to semiquinone via (mitochondrial ubiquinone oxidore-ductase) which can then be oxidized by oxygen-producing superoxide anion radicals (Darakhshan et al. [2015](#page12)). Cells exposed to thymoquinone produces superoxide dismutation (dismutase) which is present in the mitochondrial matrix, generates hydrogen peroxide, which leads to the formation of disulphide bond in adenine nucleotide transporter, thereby, inducing the formation of permeability transition pores and reducing CM-H2DCF oxidation rate, trig-gering programmed cell death in the process (Kroemer and Reed [2000](#page13); Martinovich et al. [2016](#page13)).

Isothiocyanates of pawpaw and mustard seeds

The allyl isothiocyanate exposure causes damages to the cell membrane of bacteria by creating pores which causes leakage of substances in the cytoplasm,

123

Agroforest Syst

inactivating the functional enzymes, and disrupting the cellular metabolic reactions, create homeostatic pressure and causes increased b-galactosidase activity of bacteria (Dufour et al. [2015](#page12); Clemente et al. [2016](#page12)). The isothiocyanates disrupt the redox homeostasis of the cells, both via a long lasting adaptive response that relies on the activation of transcription of antioxidant and repairs enzymes (Jeong et al. [2005](#page13)), by diminish-ing availability of intracellular GSH (Zhang [2000](#page15); Zhang et al. [2005](#page15)), inhibit glutathione reductases (Hu et al. [2007](#page13)). The potency of ITC is dose dependent in that at high concentration, function of mitochondrion is modified leading to release of proapoptotic cytochrome, reactive oxygen species is generated, and cell respiration is altered resulting in cell death (Dufour et al. [2012](#page12)). The isothiocyanates such as allyl isothiocyanate perform their antimicrobial activity by inducing intracellular cell cycle arrest (Zhang [2004](#page15)), inhibit microbial growth by altering protein structures (Kawakishi and Kaneko [1987](#page13); Delaquis and Mazza [1995](#page12)).

Other mechanisms of isothiocyanate action is alteration in intracellular structure as observed in Listeria monocytogenes (Ahn et al. [2001](#page12)), provocation of the protrusion of cell membrane in Aggregatibacter actinomycetemcomitans (Sofrata et al. [2011](#page14)) while allyl isothiocyanate causes enzymatic inhibition of Escherichia coli thioredoxin and acetate kinase (Lu-ciano and Holley [2009](#page13)).

Antimicrobial mode of action of fatty acid

Phospholipids of cell membranes are essential to ensure ideal environment for function of membrane protein (Murphy [1990](#page14)), sustaining membrane fluidity (Stubbs and Smith [1984](#page14)), and influences lipid raft formation (Yaqoob [2009](#page15)). Lipid rafts are subdomains of cell membranes (Calder [2012](#page12)). Poly unsaturated fatty acids influence cell behavior by altering the fatty composition of cell membrane phospholipids (Calder [2012](#page12)). In vitro and in vivo studies shows that it is possible for polyunsaturated fatty acids (n - 3) to alter structure and profile of cells lipid raft (Chapkin et al. [2008](#page12); Rockett et al. [2011](#page14)). Medium chain fatty acid like C12:0 and C14:0 are capable of performing their antimicrobial action as seen in rumen protozoa; by reducing pH, and their ability to dissociate. This is because in their dissociated form they can infiltrate

lipid membrane of cells and dissociate in the intracel-lular environment which causes microbes to struggle to maintain a neutral pH, leading to the depletion of cellular ATP as a resulting the death of the cell (Ricke [2003](#page14)). Moreover, de Pablo and De Cienfuegos ([2000](#page12)) noted that is cell/plasma membrane composition may be altered through dietary fatty acid manipulation; such that the phospholipid fatty acid composition of cell structure reflects the composition of lipids in the diets (Clamp et al. [1997](#page12)), consequently changing the fluidity of the cell membrane may change, and altering the protein associated with the membrane which act as receptor. The way in which these plant seeds and products, and essential oil perform their antimicrobial activity might be through alteration of the fatty acid composition of the microbes (gram positive or gram negative) and act synergistically alongside the inher-ent bioactive compound in the substrate known to elicit antimicrobial action. This synergistic role is between the lipid composition and active ingredient of the plant used. The potency of this depends on the rate at which the fatty acid can alter the lipid composition of the microbe’s cell membrane, or the concentration of lipid per time, or the quantity of unsaturated fatty acid. Once the cell membrane is altered cellular penetration of the active ingredient might be possible due to ease of binding. This is probably the reason why antimicrobial potency of plant or plant extract increas-ing with increasing concentration of bioactive ingredient.

However, excessive increase in the plant extract also increases the fatty acid composition of diets beyond beneficial level which consequently reduce the immune system; by lymphocyte and cytokine synthe-sis reduction, modifying natural killer cell activity and increasing phagocytic activity (de Pablo and de Cienfuegos [2000](#page12)). This could be the reason why high concentration of herbs, spices, essential oil, medicinal plants, usually results in lower performance, and lower WBC counts, due to reducing immune system. This is because nutrient that could have been used for production (meat, egg, milk production) are diverted for body maintenance and immune system repair. High concentration of medicinal plants will not only affect pathogenic microbes, it will also affect benefi-cial commensal microbes leading to counter production.

123

Agroforest Syst

Effect on ecto and endo parasites

Chicken gut could be contaminated by gastro intesti-nal parasites such as worms (Syngamus sp. Heterakis sp. Trichostrongylus sp. and Ascaridia sp.) (Nideou et al. [2017](#page14)) which would affect the health and growth rate of animals because there would be unwelcomed nutrient diversion in the body. Among helminths, nematodes are the most important parasite group of poultry both in terms of number of species and extent of damage they cause (Ogbaje et al. [2012](#page14)). Kerman-shai et al. ([2001](#page13)) reported that the worm destruction bioactive ingredient in pawpaw seed is benzyl isoth-iocyanate, papain, and cysteine proteinases enzymes distributed in different plant parts (Stepek et al. [2007](#page14)). The mechanism of action of benzyl isothiocyanate, papain and cystein proteinases enzymes on helminth inhibition of energy metabolism, parasite motility and destruction of protective worm cuticle respectively (Kermanshai et al. [2001](#page13); Stepek et al. [2007](#page14)).

In the gastrointestinal tract, mature worms are involved in antiperistaltic movements; ingest nutrients generated from digestion and produce species specific eggs (Nideou et al. [2017](#page14)). Feroza et al. ([2017](#page13)) infected 2000 egg/bird, and the birds were treated with pawpaw and neem seeds. On day 28, egg per gram was 1705.2 in control versus 1013 in pawpaw versus 1416.3 neem seeds, whereas on day 35, control pawpaw and neem seeds were 2166.2, 233 and 399.75 egg/g respectively. The result shows that pawpaw seeds have higher parasitic egg reducing ability by killing the parasites, and inhibiting the growth the parasitic eggs. This may be attributed to the bioactive factor in the plant seeds which has both parasite killing and anti-oviposition properties.

Anticestodal efficacy of N. sativa Linn. seeds (Kalonji), were observed when children naturally infected with cestode worm had percentage reductions in the fecal eggs per gram counts when given Black cumin seeds through oral administration (Forouzanfar et al. [2014](#page13)). In another study, Mahmoudvand et al. ([2014](#page13)) exposed protoscoleces Hydatid Cysts to vary-ing level (10, 1.0, 0.1, 0.01 mg/ml) of N. sativa Linn. essential oil. 10 mg/ml exposure led to 100% mortal-ity of the cyst within 10, 20, 30 and 60 min), 1 mg/ml concentration of essential oil led to 100% death in 20, 30, 60 min exposure. Highest death percentage for 0.1 mg/ml and 0.01 mg/ml was 76.6% and 56.6% in 60 min respectively. This indicates that elimination of

protoscoleces hydatid cyst with N. sativa Linn. essential oil is dose dependent. Similarly, 1 mg/ml of thymoquinone led 100% mortality of hydatid cyst in 10 min, 0.5 mg/ml led to 100% death of the hydatid cyst within 20 min, 0.25 mg/ml led to 100 and 96.3% death in 60 and 30 min respectively. 0.125 mg/ml thymoquinone led to 87.3% death of hydatid cyst in 60 min. From the result above large and small ruminant suffering from hydatid might be supple-mented with thymoquinone and essential oil at higher level (1 and 10 mg/ml) so that they would be enough to reach the liver after absorption in the gut.

In the study of Kermanshai et al. ([2001](#page13)) 12–24 lM (containing 0.0006 of benzyl isothiocyanate) (roughly equivalent to 1.8–3.7 mg of papaya seeds/l) aqueous papaw seeds extract was enough to kill more than 90% of Caenorhabditis elegans while the oil extract containing 0.196 M of benzyl isothiocyanate required 16.39 lM to kill more than 90% of Caenorhabditis elegans in 0.5 ml nematode assay within 4–5 h. The benzyl isothiocyanate standard (Commercially avail-able, 98% pure) containing 7.46 M of benzyl isothio-cyanate required 15.30 lM to kill more than 90% of C. elegans. The reason for fast response in pawpaw seeds extract may be due to other bioactive compound or phytochemical which acted alongside or as comple-mentary to the benzyl isothiocyanate. This substance could be detrimental to both beneficial and harmful gut microbes (Kermanshai et al. [2001](#page13)). Thus while treatment with papaya seeds might eliminate patho-genic intestinal bacteria, it could also affect commen-sal bacteria.

In developing countries, grazing animals are con-stantly affected by different type of endo-parasites which affects their performance due to the competition between the host and this parasite for nutrients. Thus, eliminating these parasites could improve production parameters. In the study of Ameen et al. ([2010](#page12)), west African Dwarf sheep were given 300 mg of dry seeds and aqueous extract 1:10 ml of pawpaw seed was given for 3 days at 2 weeks interval. Papaya seeds caused a 91.3% reduction of Haemonchus contortus, while the aqueous extract reduced by 100% in 4 weeks. There was 82.2% in Trichostrongylus sp. in pawpaw seed while the extract reduced it by 100% in 4 weeks, while there was 100% reduction in Strongy-loides sp. and Ostertagia sp. in 4 weeks in both seeds and aqueous extract. This effectiveness of pawpaw seeds in reducing the helminth may be attributed to the

123

Agroforest Syst

benzyl isothiocyanate, papain and cysteine proteinases enzymes in the pawpaw seeds which is responsible for killing or inhibition of the egg and the parasites in the gut. One of the beneficial effect of reducing helminth in the gut is the added advantage of nutrient availability to the host. Thus eliminating gut parasite might lead to improved production parameters.

Ecto parasites

Rhipicephalus (Boophilus) microplus is a common and widely distributed tick that serves as a major channel for transmitting pathogens such as Babesia bigemina and Anaplasma marginale (Shyma et al. [2014](#page14)). The ineffectiveness of acaricidal as a conse-quence of frequent application and improper dosage, resulted in the resistance of the ticks, and discovering new acaricidal is going to be difficult and cost intensive (NRC [1986](#page14)). In vitro studies of Shyma et al. ([2014](#page14)) investigated the influence of methanol extract of pawpaw seeds on cattle tick Rhipicephalus (Boophilus) microplus, 100 mg/ml of pawpaw seeds extract killed 93.3% of adults in 15 days, inhibiting mean egg mass per replicate, prevented their repro-duction, inhibited completely their oviposition, and killed 82.2% of their larvae while 25 mg/ml of methanol pawpaw extract inhibited killed 46.67% of adults within 15 days, 0.017 mean egg mass per replicate, 0.031 reproduction index, 94.7% inhibition of their oviposition, and killed 64% of their larvae. From the result obtained pawpaw seeds possessed acaricidal properties. This is going to be very useful in tropical countries and in particular, sub Saharan African regions where nomadic system of ruminant production is still practiced. In this region, grazing ruminants are affected by tick and this is evident in dry season when cattle egret move with cattle in order to pick on ecto-parasites. Moreover, during rainy season cattle pick up tick when they are grazing which suck their blood and if in excess could damage the skin, cause secondary infection and might cause anemia. Thus, methanol or aqueous extract of pawpaw seeds could be applied topically on animal skin or sprayed on some ‘‘inner’’ part of the body of cattle where tick hide to reduce their population and inhibit their proliferation.

Others

Due to sceptism to the use of mustard, further processes in order to reduce the glucosinolates might endear farmers to consider it. Rakariyatham and Sakorn ([2002](#page14)) investigation revealed that incubation of mustard seeds with Aspergillus sp. NR-4201 is cable of degrading glucosinolate and could be elim-inated within 48 h. This could be useful in increasing protein availability/options for farmers’ residing in developing countries. However care must be taken due to allylcyanide produced as a byproduct of glucosino-late degradation. Duncan and Milne ([1992](#page12)) suggested that allylcyanide are less toxic to sheep due to ruminal microbial degradation of this compound. This should also be applicable to other domesticated ruminants (cattle, goat and buffalo).

Conclusions

Inclusion of the seeds of black cumin, pawpaw and mustard are capable of antimicrobial functions, reduc-ing pathogenic microbes in the gut, microbial popu-lation in livestock. All the plants used have strong antimicrobial properties. Ten mg/ml and 1 mg/ml of Black seeds essential oil and thymoquinone respec-tively are capable of killing hydatid cyst within 10 min. The microbial growth stimulating potential of sinapine—a derivative of sinapic acid should be research to find it potency as probiotics. Furthermore, inclusion of 15% mustard oil in vitro reduced methane production without affecting fermentation processes or by product and it reduced protozoa population. The unique properties of pawpaw seed is its strong potency against ecto and endoparasites. Haemonchus contor-tus, Trichostrongylus spp., Strongyloides spp., Ostertagia spp., Caenorhabditis elegans, Eimeria spp., Heterakis gallinarum, Ascaridia galli, Tri-chostrongylus tenuis. Spraying of pawpaw seeds on animal would kill or inhibit the proliferation of Rhipicephalus (Boophilus) microplus eggs. Any plant that must be classified as phytogenic feed additive should be able perform at least antimicrobial functions alongside other function with about 2% of its presence in diet, while ingredient that perform same function in above 3% should be regarded feed ingredient with multifaceted functions.

123

Agroforest Syst

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Abd El-Hack ME, Mahgoub SA, Hussein MMA, Saadeldin IM (2018) Improving growth performance and health status of meat-type quail by supplementing the diet with black cumin cold-pressed oil as a natural alternative for antibi-otics. Environ Sci Pollut Res 25:1157–1167

Abul-Fadl M, El-Badry N, Ammar M (2011) Nutritional and chemical evaluation for two different varieties of mustard seeds. World Appl Sci J 15:1225–1233

Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, Damanhouri ZA, Anwar F (2013) A review on ther-apeutic potential of Nigella sativa: a miracle herb. Asian Pac J Trop Biomed 3:337–352

Ahn E, Kim J, Shin D (2001) Antimicrobial effects of allyl isothiocyanate on several microorganisms. Korean J Food Sci Technol 31:206–211

Akhtar MS (1988) Anthelmintic evaluation of indigenous medicinal plants for veterinary usage. Final report of the PARC Research Project (1985-86), University of Agri-culture Pakistan

Ameen SA, Adedeji OS, Ojedapo LO, Salihu T, Fabusuyi CO (2010) Anthelmintic potency of pawpaw (Carica papaya) seeds in West African Dwarf (WAD) sheep. Glob Vet 5:30–34

Ansari AA, Hassan S, Kenne L, Atta-ur-Rehman S, Wehler T (1988) Structural studies on a saponin isolated from Nigella sativa. Phytochemistry 27:3977–3979

Augustin JM, Kuzina V, Andersen SB, Bak S (2011) Molecular activities, biosynthesis and evolution of triterpenoid saponins. Phytochemistry 72:435–457

Badary OA, Taha RA, Gamal El-Din AM, Abdel-Wahab MH (2003) Thymoquinone is a potent superoxide anion scav-enger. Drug Chem Toxicol 26:87

Barroso PTW, de Carvalho PP, Rocha TB, Pessoa FLP, Aze-vedo DA, Mendes MF (2016) Evaluation of the composi-tion of Carica papaya L. seed oil extracted with supercritical CO2. Biotechnol Rep 11:110–116

Biomin (2016) What’s wrong with my herd? Part 2: endotoxins science and solutions: a magazine of Biomin . Ruminant issue #37:1–9

Calder PC (2012) Mechanisms of action of (n - 3) fatty acids. J Nutr 142:592–599

Cartea ME, Francisco M, Soengas P, Velasco P (2010) Phenolic compounds in brassica vegetables. Molecules 16:251–280 Cetin-Karaca H (2011) Evaluation of natural antimicrobial phenolic compounds against foodborne pathogens. Dis-

sertation, University of Kentucky

Chaieb K, Kouidhi B, Jrah H, Mahdouani K, Bakhrouf A (2011) Antibacterial activity of thymoquinone, an active principle of Nigella sativa and its potency to prevent bacterial bio-film formation. BMC Complement Altern Med 11:29

Chapkin RS, Wang N, Fan YY, Lupton JR, Prior IA (2008) Docosahexaenoic acid alters the size and distribution of

cell surface microdomains. Biochim Biophys Acta 1778:466–471

Clamp AG, Ladha S, Clark DC, Grimble RF, Lund EK (1997) The influence of dietary lipids on the composition and membrane fluidity of rat hepatocyte plasma membrane. Lipids 32:179–184

Clemente I, Aznar M, Silva F, Nerı´n C (2016) Antimicrobial properties and mode of action of mustard and cinnamon essential oils and their combination against foodborne bacteria. Innov Food Sci Emerg Technol 36:26–33

Coleman JJ, Okoli I, Tegos GP, Holson EB, Wagner FF, Hamblin MR, Mylonakis E (2010) Characterization of plant-derived saponin natural products against Candida albicans. Am Chem Soc Chem Biol 5:321–332

Cowan MM (1999) Plant products as antimicrobial agents. Clin Microbiol Rev 12:564–582

Cueva C, Moreno-Arribas MV, Martı´n-Alvarez PJ, Bills G, Vicente MF, Basilio A, Rivas CL, Requena T, Rodrı´guez JM, Bartolome´ B (2010) Antimicrobial activity of phenolic acids against commensal, probiotic and pathogenic bacte-ria. Res Microbiol 161:372–382

Cui W, Eskin NA (1998) Processing and properties of mustard products and components. In: Mazza G (ed) Functional foods: biochemical and processing aspects. Technomic Publishing, Lancaster, pp 235–264

Cushnie TPT, Lamb AJ (2005) Antimicrobial activity of fla-vonoids. Int J Antimicrob Agents 26:343–356

Cushnie TPT, Lamb AJ (2011) Recent advances in under-standing the antibacterial properties of flavonoids. Int J Antimicrob Agents 38:99–107

Dada FA, Nzewuji FO, Esan AM, Oyeleye SI, Adegbola VB (2016) Phytochemical and antioxidant analysis of aqueous extracts of unripe pawpaw (Carica papaya Linn.) fruit’s peel and seed. Int J Recent Res Appl Stud 27:68–71

Darakhshan S, Bidmeshki A, Pour A, Colagar H, Sisakhtnezhad S (2015) Thymoquinone and its therapeutic potentials. Pharm Res 138:95–96

De Pablo MA, De Cienfuegos GA (2000) Modulatory effects of dietary lipids on immune system functions. Immunol Cell Biol 78:31–39

Delaquis PJ, Mazza G (1995) Antimicrobial properties of isothiocyanates in food preservation. Food Technol 49:73–78

Desai SD, Saheb SH, Das KK, Haseena S (2015) Phytochemical analysis of Nigella sativa and it‘s antidiabetic effect. J Pharm Sci Res 7:527–532

Dufour V, Alazzam B, Ermel G, Thepaut M, Rossero A, Tresse O, Baysse C (2012) Antimicrobial activities of isothio-cyanates against Campylobacter jejuni isolates. Front Cell Infect Microbiol 53:1–13

Dufour V, Stahl M, Baysse C (2015) The antibacterial properties of isothiocyanates. Microbiology 161:229–243

Duncan AJ, Milne JA (1992) Rumen microbial degradation of allyl cyanide as a possible explanation for the tolerance of sheep to Brassica-derived glucosinolates. J Sci Food Agric 58:15–19

El-Nagerabia SA, Al-Bahryb SN, El-shafieb AE, Al-Hilalib S (2012) Effect of Hibiscus sabdariffa extract and Nigella sativa oil on the growth and aflatoxin B1 production of Aspergillus flavus and Aspergillus parasiticus strains. Food Control 25:59–63

123

Agroforest Syst

Engels C, Schieber A, Ga¨nzle MG (2012) Sinapic acid deriva-tives in defatted oriental mustard (Brassica juncea L.) seed meal extracts using UHPLC-DAD-ESI-MS and identifi-cation of compounds with antibacterial activity. Eur Food Res Technol 234:535–542

Fahey JW, Zalcmann AT, Talalay P (2001) The chemical diversity and distribution of glucosinolates and isothio-cyanates among plants. Phytochemistry 56:5–51

Fahmi R (2016) Antioxidant and antibacterial properties of endogenous phenolic compounds from commercial mus-tard products. Dissertation, University of Manitoba

Feroza S, Arijo AG, Zahid IR (2017) Effect of papaya and neem seeds on Ascaridia galli infection in broiler chicken. Pak J Nematol 35:105–111

Forouzanfar F, Bazzaz BSF, Hosseinzadeh H (2014) Black cumin (Nigella sativa) and its constituent (thymoquinone): a review on antimicrobial effects. Iran J Basic Med Sci 17:929–938

Frazie MD, Kim MJ, Ku KM (2017) Health-promoting phyto-chemicals from 11 mustard cultivars at baby leaf and mature stages. Molecules 1:1–13

Gharby S, Harhar H, Guillaume D, Roudani A, Boulbaroud S, Ibrahimi M, Ahmad M, Sultana S, Hadda TB, Chaf-chaouni-Moussaoui I, Charrouf Z (2015) Chemical inves-tigation of Nigella sativa L. seed oil produced in Morocco. J Saudi Soc Agric Sci 14:172–177

Goel S, Mishra P (2018) Thymoquinone inhibits biofilmfor-mation and has selective antibacterial activity due to ROS generation. Appl Microbio Biotechnol 102:1955–1967

Goosen TC, Mills DE, Hollenberg PF (2001) Effects of benzyl isothiocyanate on rat and human cytochromes P450: identification of metabolites formed by P450 2B1. J Phar-macol Exp Ther 296:198–206

Herzallah S, Holley R (2012) Determination of sinigrin sinalbin, allyl-and benzyl isothiocyanates by RP-HPLC in mustard powder extracts. LWT Food Sci Technol 47:293–299

Høiby N, Bjarnsholt T, Givskov M, Molin S, Ciofu O (2010) Antibiotic resistance of bacterial biofilms. Int J Antimicrob Agents 35:322–332

Hu Y, Urig S, Koncarevic S, Wu X, Fischer M, Rahlfs S, Mersch-Sundermann V, Becker K (2007) Glutathione-and thioredoxin-related enzymes are modulated by sulfur-containing chemopreventive agents. Biol Chem 388:1069–1081

Jamroz D, Kamel C (2002) Plant extracts enhance broiler per-formance. In non ruminant nutrition: antimicrobial agents and plant extracts on immunity, health and performance. J Anim Sci 80:41

Javed S, Shahid AA, Haider MS, Umeera A, Ahmad R, Mushtaq S (2012) Nutritional, phytochemical potential and phar-macological evaluation of Nigella sativa (Kalonji) and Trachyspermum ammi (Ajwain). J Med Plants Res 6:768–775

Jeong WS, Keum YS, Chen C, Jain MR, Shen G, Kim JH, Li W, Kong AN (2005) Differential expression and stability of endogenous nuclear factor E2-related factor 2 (Nrf2) by natural chemopreventive compounds in HepG2human hepatoma cells. J Biochem Mol Biol 38:167–176

Kakimoto Y, Armstrong MD (1962) The phenolic amines of human urine. J Biol Chem 237:208–214

Kawakishi S, Kaneko T (1987) Interaction of proteins with allyl isothiocyanate. J Agric Food Chem 35:85–88

Kermanshai R, McCarry BE, Rosenfeld J, Summers PS, Weretilnyk EA, Sorger GJ (2001) Benzyl isothiocyanate is the chief or sole anthelmintic in papaya seed extracts. Phytochemistry 57:427–435

Khan MA (1999) Chemical composition and medicinal prop-erties of Nigella sativa Linn. Inflammopharmacology 7:15–35

Khan SH, Ansari J, Haq A, Abbas G (2012) Black cumin seeds as phytogenic product in broiler diets and its effects on performance, blood constituents, immunity and caecal microbial Population. Ital J Anim Sci 11:438–444

Kroemer G, Reed JC (2000) Mitochondrial control of cell death. Nat Med 6:513

Kubo I, Muroi H, Kubo A (1995) Structural functions of antimicrobial long-chain alcohols and phenols. Bioorg Med Chem Lett 3:873–880

Kumar NS, Devi SPS (2017) The surprising health benefits of papaya seeds: a review. J Pharmacogn Phytochem 6:424–429

Kumara SS, Huat BT (2001) Extraction, isolation and charac-terization of anti-tumour principle, alpha-hedrin, from the seeds of Nigella sativa. Planta Med 67:29–32

Larsen PO (1965) Occurrence of p-hydroxybenzylamine in white mustard (Sinapis alba L.). Biochem Biophys Acta 107:134–136

Lohidas J, Manjusha S, Jothi GGG (2015) Antimicrobial activities of Carica papaya L. Plant Arch 15:1179–1186

Luciano FB, Holley RA (2009) Enzymatic inhibition by allyl isothiocyanate and factors affecting its antimicrobial action against Escherichia coli O157:H7. Int J Food Microbiol 131:240–245

Lutterodt H, Luther M, Slavin M, Yin JJ, Parry J, Gao JM, Yu L (2010) Fatty acid profile thymoquinone content, oxidative stability and antioxidant properties of cold-pressed black cumin seed oils. LWT Food Sci Technol 43:1409–1413

Mah T-F, O’Toole GA (2001) Mechanisms of biofilm resistance to antimicrobial agents. Trends Microbiol 9:34–39 Mahmoudvand H, Dezaki ES, Kheirandish F, Ezatpour B,

Jahanbakhsh S, Harandi MF (2014) Scolicidal effects of black cumin seed (Nigella sativa) essential oil on hydatid cysts. Korean J Parasitol 52:653–659

Maisarah AM, Asmah R, Fauziah O (2014) Proximate analysis, antioxidant and antiproliferative activities of different parts of Carica papaya. J Nutr Food Sci 4:1043–1048

Mandal P, Sinha Babu SP, Mandal NC (2005) Antimicrobial activity of saponins from Acacia auriculiformis. Fitoter-apia 76:462–465

Martinovich GG, Martinovich IV, Vcherashniaya AV, Shadyro OI, Cherenkevich SN (2016) Thymoquinone a biologically active component of Nigella sativa, induces mitochondrial production of reactive oxygen species and programmed death of tumor cells. Biophy 61:963–970

Mason TL, Wasserman BP (1987) Inactivation of red beet betaglucan synthase by native oxidized phenolic com-pounds. Phytochemistry 26:2197–2202

Melzig MF, Bader G, Loose R (2001) Investigations of the mechanism of membrane activity of selected triterpenoid saponins. Planta Med 67:43–48

123

Agroforest Syst

Merfort I, Wary V, Barakat H, Hussain A, Nawwar AM (1997) Flavonol triglycosides from seeds of Nigella sativa. Phy-tochemistry 46:359–363

´ ´ ˇ

Merkl R, Hradkova I, Filip SJ (2010) Antimicrobial and antioxidant properties of phenolic acids alkyl esters. Czech J Food Sci 28:275–279

Mitsch P, Zitterl-Eglseer K, Kohler B, Gabler C, Losa R, Zim-pernik I (2004) The effect of two different blends of essential oil components on the proliferation of Clostrid-ium perfringens in the intestines of broiler chickens. Poult Sci 83:669–675

Moreno S, Scheyer T, Romano CS, Vojnov AA (2006) Antioxidant and antimicrobial activities of rosemary extracts linked to their polyphenol composition. Free Rad Res 40:223–231

Murphy MG (1990) Dietary fatty acids and membrane protein function. J Nutr Biochem 1:68–79

Nagi MN, Mansour MA (2000) Protective effect of thymo-quinone against doxorubicin-induced cardiotoxicity in rats: a possible mechanism of protection. Pharm Res 41:283

National Research Centre (1986) Pesticide resistance: strategies and tactics for management. National Academy Press, Washington, p 471

Nideou D, Soedji K, Teteh A, Decuypere E, Gbeassor M, Tona K (2017) Effect of Carica Papaya seeds on gastro-in-testinal parasites of pullet and production parameters. Int J Probiotics Prebiotics 12:89–96

Obi RK, Nwanebu FC, Ndubuisi UU, Orji NM (2009) Antibacterial qualities and phytochemical screening of the oils of Cucurbita pepo and Brassica nigra. J Med Plants Res 3:429–432

Ogbaje CI, Agbo EO, Ajanusi OJ (2012) Prevalence of As-caridia galli, Heterakis gallinarum tapeworm infections in birds slaughtered in Makurdi Township. Int J Poult Sci 11:103–105

Okigbo RN, Anuagasi CL, Amadi JE (2009) Advances in selected medicinal and aromatic plants indigenous to Africa. J Med Plants Res 3:086–095

Osbourn AE (1996) Preformed antimicrobial compounds and plant defense against fungal attack. Plant Cell 8:1821–1831 Paarakh MP (2010) Nigella sativa Linn. Indian J Nat Prod

Resour 1:409–429

Parikh H, Khanna A (2014) Pharmacognosy and phytochemical analysis of Brassica juncea seeds. Pharmacogn Res 6:47–54

Patra AK (2012) An overview of antimicrobial properties of different classes of phytochemicals. In: Patra AK (ed) Dietary phytochemicals and microbes. Springer, New York, pp 1–32

Pavarini DP, Pavarini SP, Niehues M, Lopes NP (2012) Exogenous influences on plant secondary metabolite levels. Anim Feed Sci Technol 176:5–16

Peter JK, Kumar Y, Pandey P, Masih H (2014) Antibacterial activity of seed and leaf extract of Carica Papaya var. Pusa dwarf Linn. IOSR J Pharm Biol Sci 9:29–37

Peterson HL (1970) Evaluation of mustard meal as a source of supplemental protein. Dissertation, Montana State University

Polat U (2010) The effects on metabolism of glucosinolates and theirs hydrolysis products. J Biol Environ Sci 4:39–42

Rakariyatham N, Sakorn P (2002) Biodegradation of glucosi-nolates in brown mustard seed meal (Brassica juncea) by Aspergillus sp. NR-4201 in liquid and solid-state cultures. Biodegradation 13:395–399

Ricke SC (2003) Perspectives on the use of organic acids and short chain fatty acids as antimicrobials. Poult Sci 82:632–639

Rockett BD, Franklin A, Harris M, Teague H, Rockett A, Shaikh SR (2011) Lipid raft organization is more sensitive to disruption by (n - 3) PUFA than nonrafts of EL4 and B cells. J Nutr 141:1041–1048

Sahoo A, Soren NM (2012) Phytochemicals and gut microbial populations in non-ruminants. In: Patra AK (ed) Dietary phytochemicals and microbes. Springer, New York, pp 379–381

Salihu MD, Junaidu AU, Magaji AA, Abubakar MB, Adamu AY, Yakubu AS (2009) Prevalence of Campylobacter in poultry meat in Sokoto, Northwestern Nigeria. J Public Health Epidemiol 1:041–045

Sampedro J, Valdivia ER (2014) New antimicrobial agents of plant origin. In: Villa TG, Veiga-Crespo P (eds) Antimi-crobial compounds. Springer, Berlin, pp 83–114

Sharma NK, Ahirwar D, Jhade D, Gupta S (2009) Medicinal and pharmacological potential of Nigella sativa: a review. Ethnobot Rev 13:946–955

Shyma KP, Gupta JP, Ghosh S, Patel KK, Singh V (2014) Acaricidal effect of herbal extracts against cattle tick Rhipicephalus (Boophilus) microplus using in vitro stud-ies. Parasitol Res 113:1919–1926

Simo˜es M, Lemos M, Simo˜es LC (2012) Phytochemicals against drug-resistant microbes. In: Patra AK (ed) Dietary phytochemicals and microbes. Springer, New York, pp 379–381

Sinha Babu SP, Sarkar D, Ghosh NK, Saha A, Sukul NC, Bhattacharya S (1997) Enhancement of membrane damage by saponins isolated from Acacia auriculiformis. Jpn J Pharmacol 75:451–454

Sofrata A, Santangelo EM, Azeem M, Borg-Karlson AK, Gustafsson A, Putsep K (2011) Benzyl isothiocyanate, a major component from the roots of Salvadora persica is highly active against Gram-negative bacteria. PLoS ONE 6:23045

Sporsheim B, Øverby A, Bones AM (2015) Allyl isothiocyanate inhibits actin-dependent intracellular transport in Ara-bidopsis thaliana. Int J Mol Sci 16:29134–29147

Stepek G, Lowe AE, Buttle DJ, Duce IR, Behnke JM (2007) The anthelminthic efficacy of plant-derived cysteine pro-teinases against the rodent gastrointestinal nematode, Heligmosomoides polygyrus in vivo. Parasitology 134:1409–1419

Stubbs CD, Smith AD (1984) The modification of mammalian membrane polyunsaturated fatty acid composition in relation to membrane fluidity and function. Biochim Bio-phy Acta 779:89–137

Suarez M, Haenni M, Canarelli S, Fisch F, Chodanowski P, Servis C, Michielin O, Freitag R, Moreillon P, Mermod N (2005) Structure-function characterization and optimiza-tion of a plant-derived antibacterial peptide. Antimicrob Agents Chemother 49:3847–3857

123

Agroforest Syst

Tang CS, Bhothipaksa K, Frank HA (1972) Bacterial degrada-tion of benzyl isothiocyanate. Appl Microbiol 23:1145–1148

Teirlynck E, Bjerrum L, Eeckhaut V, Huyghebaert G, Pasmans F, Haesebrouck F, Dewulf J, Ducatelle R, Van Immerseel F (2009) The cereal type in feed influences gut wall mor-phology and intestinal immune cell infiltration in broiler chickens. Br J Nutr 102:1453–1461

Tesaki S, Tanabe S, Ono H, Fukushi E, Kawabata J, Watanabe M (1998) 4-Hydroxy-3-nitrophenyllactic and sinapic acids as antibacterial compounds from mustard seeds. Biosci Biotechnol Biochem 62:998–1000

Tzounis X, Vulevic J, Kuhnle GG, George T, Leonczak J, Gibson GR, Kwik-Uribe C, Spencer JP (2008) Flavanol monomer-induced changes to the human fecal microflora. Br J Nutr 99:782–792

Vandeputte OM, Kiendrebeogo M, Rasamiravaka T, Ste´vigny C, Duez P, Rajaonson S, Diallo B, Mol A, Baucher M, El Jaziri M (2011) The flavanone naringenin reduces the production of quorum sensing-controlled virulence factors in Pseudomonas aeruginosa PAO1. Microbiology 157:2120–2132

Windisch W (2009) Alternatives to antibiotic growth promot-ers—what options do we have? In: Trends in animal nutrition where are the boundaries? Delacon dossier, no. 3, pp 1–36

Windisch W, Schedle K, Plitzner C, Kroismayr A (2008) Use of phytogenic products as feed additives for swine and poul-try. J Anim Sci 86:140–148

Ya C, Gaffney SH, Lilley TH, Haslam E (1988) Carbohy-dratepolyphenol complexation. In: Hemingway RW, Karchesy JJ (eds) Chemistry and significance of condensed tannins. Plenum Press, New York, p 553

Yamato Y, Gayor RB (2002) Therapeutic potential of inhibitory of the NF.KB pathway in the treatment of inflammation and cancer. J Clin Investig 1:493–503

Yaqoob P (2009) The nutritional significance of lipid rafts. Annu Rev Nutr 29:257–282

Yessuf AM (2015) Phytochemical extraction and screening of bio active compounds from black cumin (Nigella Sativa) seeds extract. Am J Life Sci 3:358–364

Zhang Y (2000) Role of glutathione in the accumulation of anticarcinogenic isothiocyanates and their glutathione conjugates by murine hepatoma cells. Carcinogenesis 21:1175–1182

Zhang Y (2004) Cancer-preventive isothiocyanate: measure-ment of human exposure and mechanism of action. Mutat Res Fundam Mol Mech 555:173–190

Zhang Y, Lewis K (1997) Fabatins: new antimicrobial plant peptides. FEMS Microbiol Lett 149:59–64

Zhang Y, Chen J, Chen Y, Dong J, Wei Q, Lou J (2005) Envi-ronmental mycological study and allergic respiratory dis-ease among tobacco processing workers. J Occup Health 47:181–187

Zhang J, Van L, Steven G, Ju J, Liu W, Dorrestein PC, Li W, Kelleher NL, Shen B (2008) A phosphopantetheinylating polyketide synthase producing a linear polyene to initiate enediyne antitumor antibiotic biosynthesis. Proc of Natl Acad Sci USA 105:1460–1465

123

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