Journal of Pharmaceutical, Chemical and Biological Sciences
ISSN: 2348-7658
Jun-August 2014; 2(2):77-85
Available online at http://www.jpcbs.info

Review Article

Mechanisms of Antimicrobial Actions of Phytochemicals against Enteric Pathogens – A Review

Omojate Godstime C[1], Enwa Felix O*[1], Jewo Augustina O[2], Eze Christopher O[1]

[1]Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Delta State University Abraka, Nigeria.
[2]Department of Microbiology, Faculty of Science, Delta State University, Abraka. Nigeria

*** Corresponding Author**

Received: 14 June 2014 Revised: 17 June 2014 Accepted: 27 June 2014

ABSTRACT

Plants produce a diverse array of secondary metabolites, many of which have antimicrobial activities against some pathogenic microorganisms that are implicated in enteric infections. Some of these compounds are constitutive, existing in healthy plants in their biologically active forms and they elicit chemotherapeutic or chemoprophylactic properties against a wide range of infectious enteric diseases. Since the antimicrobial resistance pattern are dependent partly, upon their modes of action, this current research was carried out to suggest alternative mechanisms of phytochemicals' antimicrobial action to combat the emerging enteric microbial strains that are becoming refractory to the available allopathic chemotherapeutics.Many mechanisms of antimicrobial action of phytochemicals have been suggested by different researchers but there exists uncertainties as to the molecular basis for their modes of action. Some phytochemicals may act by inhibiting microbial growth, inducing cellular membrane perturbations, interference with certain microbial metabolic processes, modulation of signal transduction or gene expression pathways. Although this is a preliminary research, it is suggested that the molecular basis for the modes of action of plant-based antibiotics be ascertained and to determine if these phytochemicals would exhibit these mechanisms in vitro on sensitive enteric pathogenic microorganisms.

Keywords: Enterotoxigenic; phytochemicals; pathogens; enteric; free radicals.

INTRODUCTION

Despite the advances made by the pharmaceutical industry in the development of novel and highly effective therapeutic regimes for the treatment gastrointestinal diseases, there has been a significant increase in the incidence of enteric disorders in the developing as well as the affluent countries of the world.

The gastrointestinal tract represents a suitable ecosystem for enteric bacterial pathogens possibly due to the mucous nature and the presence of

macro and micro-nutrients on the epithelial cell lining. It provides shelter from the outside world, yet is easily accessible, provides an array of nutrients, and is less likely to elicit an immunogenic response upon bacterial invasion. Some enteric bacterial species can be highly pathogenic when they invade and colonize the digestive tract, thereby causing gastrointestinal disorders which range from diarrhoea, gastroenteritis, shigellosis, salmonellosis, to life threatening consequences.

Many bacterial species implicated in gastrointestinal diseases (the *enterobacteriaceae* family) include *Clostridium difficile, Salmonella enterica, S. enteritidis, S. Heidelberg, S. typhymurium, Shigella dysenteriae, Klebsiella spp., Enterobacter spp., Vibrios spp., Yersinia pestis, Proteus spp, Bacillus cereus, Helicobacter pylori, Campylobacter coli, Campylobacter jejuni*, enterotoxigenic *Escherichia coli,among others.*

Clostridium difficile infection results in severe diarrhea and about 25,000 cases are reported every year in the UK, and in 2008 it was linked to over 8,000 deaths (five times more than MRSA for that year).Studies on the genetic analysis of the region coding for the S-layer that surrounds *C. difficile* cells have been carried out and it is suggested that this represents a crucial point of contact with the host.

All strains of *Salmonella enterica* cause disease, but some are more pathogenic than others. In a study, the whole genomes of the two most severe serotypes of *Salmonella enterica*: Typhi and Paratyphi A which cause typhoid and paratyphoid fever, respectively, were found to be responsible for many mortalities.

*Bacillus cereus*is a group of mostly non-pathogenic bacteria, although some strains can cause food-borne illnesses in animals. *Helicobacter pylori* differs from other enteric bacterial pathogens, in that it is the only bacteria able to live in the stomach (rather than the intestines) and survive in this acidic ecosystem for many years. Although it can be carried asymptomatically for decades, it can eventually lead to serious complications including hundreds of thousands of cases of gastric cancer every year.

Campylobacter jejuni and *Campylobacter coli* are the main causes of human gastroenteritis, with infection often originating from farmed cattle, swine or poultry. The evolutionary processes by which lineages of *Campylobacter* adapt differentially to various environmental niches provide insights into its mechanisms of pathogenicity[1].

Several plant species have shown promising microbiostatic and microbiocidal activities against a range of enteric pathogenic microbionta and these are attributed to the presence of minute doses of bioactive principles referred to as phytochemicals [2]. These phytochemicals include the alkaloids, flavonoids, tannins, terpenoids, glycosides, saponins, anthraquinones, among others.

Alkaloids are the largest group of secondary plant metabolites comprising basically of nitrogen bases synthesized from amino acid building blocks with various radicals replacing one or more of the hydrogen atoms in the peptidic ring, most containing oxygen. These nitrogenous compounds act in plant defence against enteric pathogenic organisms,and are widely exploited as pharmaceuticals, psycho-stimulants, narcotics, and poisons due to their renowned biologic activities.

Glycosides are the condensation products of sugars with a host of different varieties of organic hydroxyl or thiol compounds, in such a manner that the hemiacetal moiety of the carbohydrate plays an ignoble role in the condensation reaction. Examples of glycosides includes trophanthidin from *Strophanthus*, digitoxin from *Digitalis*, barbaloin from *Aloes*, salicin from *Salix*, cantharidin from *Cantharides*, and prunasin from *Prunus.* This group of drugs is usually administered in order to promote appetite and aid digestion. Glycosides are purely bitter principles that are commonly found in plants of the *Genitiaceae* family and though they are chemically unrelated but possess the common

property of an intensely bitter taste. The bitters act on gustatory nerves, which results in increased flow of saliva and gastric juices. Chemically, the bitter principles contain thelactone group that may be diterpene lactones (as in *andrographolide*) or triterpenoids (as in *amarogentin*). Some of the bitter principles are either used as astringents due to the presence of tannic acid, as antiprotozoan, or to reduce thyroxine and metabolism. Examples include cardiac glycosides (acts on the heart), anthracene glycosides (purgative and for the treatment of skin diseases), chalcone glycoside (anticancer), amarogentin, gentiopicrin, rographolide, ailanthone and polygalin. Flavonoids are important group of polyphenols widely distributed among the plant flora. Structurally, they are made of more than one benzene ring in its structure and numerous reports support their use as antioxidants or free radical scavengers [3]. The compounds are derived from parent compounds known as flavans. Over four thousand flavonoids are known to exist and some of them are pigments in higher plants. Quercetin, kaempferol and quercitrin are common flavonoids present in nearly 70% of plants. Other groups of flavonoids include flavones, dihydroflavons, flavans, flavonols, anthocyanidins, proanthocyanidins, calchones and catechin and leucoanthocyanidins.

Phenolics, phenols or polyphenolics (or polyphenol extracts) are chemical components that occur ubiquitously as natural colour pigments responsible for the colour of fruits of plants. Phenolics in plants are mostly synthesized from phenylalanine via the action of phenylalanine ammonia lyase (PAL). They are very important to plants and have multiple functions. The most important role may be in plant defence against pathogens and herbivore predators, and thus are applied in the control of human pathogenic infections.

Saponins are compounds with 'soaplike' behaviour in water, i.e. they produce foam upon shaking. On hydrolysis, an aglycone is produced, which is called sapogenin. Saponins are extremely poisonous, as they cause heamolysis of blood and are known to cause cattle poisoning. They possess a bitter and acrid taste, besides causing irritation to mucosal membranes.

Tannins are used as antiseptic and this activity is due to presence of the phenolic group. In Ayurveda, formulations based on tannin-rich plants have been used for the treatment of enteric diseases like diarrhoea.

Terpenes are among the most widespread and chemically diverse groups of natural products. The sesquiterpene acts as irritants when applied externally and when consumed internally, their action resembles that of gastrointestinal tract irritant. A number of sesquiterpene lactones have been isolated and have been shown to elicit antibacterial and antiprotozoal properties. The sesquiterpene lactone, palasonin, isolated from *Butea monosperma* has anthelmintic activity, inhibits glucose uptakeand depletes the glycogen content in *Ascaridia galli* [3].

Since the antimicrobial resistance pattern are dependent partly, upon their modes of action, this current research was carried out to suggest alternative mechanisms of phytochemicals' antimicrobial action to combat the emerging enteric microbial strains that are becoming refractory to the available allopathic chemotherapeutics.

DISCUSSION

Phytochemicals elicit chemotherapeutic or chemoprophylactic properties against an array of infectious enteric diseases. Many mechanisms of antimicrobial action of phytochemicals have been suggested by different researchers [4-6], opined that phytochemicals may act by inhibiting microbial growth, inducing cellular membrane perturbations, interference with certain microbial metabolic processes, modulation of signal transduction or gene expression pathways.

Plant-based constituents may exhibit different modes of action against enterotoxigenic bacterial strains which range from interference with the phospholipoidal cell membranes, which has as a consequence of increasing the permeability profile and loss of cellular constituents, damage of the enzymes involved in the production of cellular energy and synthesis of structural components, and destruction or inactivation of genetic material. In general, the mechanism of action is considered to be the disturbance of the cytoplasmic membrane, disrupting the proton motive force, electron flow, active transport mechanisms, and coagulation of cell composition [7].

The mechanism of action by which the phytochemical constituents of *M. oleifera* exert their antibacterial activity might be attributed to bacterial enzyme inhibition such as the sortase inhibitory effect, DNA replication, bacterial toxin action and causing the lysis of bacterial cells. It had been suggested that pterygospermin acts by the inhibition of the transaminase enzyme and through cell membrane perturbations [8]. This, when coupled with the action of Beta lactams on the transpeptidation of the bacterial cell wall could lead to an enhanced antimicrobial effect of the combinations. Antimicrobial peptides probably interact with cellular membranes in two stages. Firstly, cationic amino acids are attracted by negative charges such as phospholipoidal groups on the surface. Secondly, hydrophobic acid and positively charged patches of the peptides interact with the aliphatic fatty acids and anionic components respectively. This induces membrane destabilizaton and bacteria are thought to be killed by the leakage of cytoplasmic contents, loss of membrane potential, change of membrane permeability, lipid distribution, the entry of peptides and the occlusion of anionic cell components or the actuation of autolytic enzymes. Tannins are polyphenols with pronounced ability to suppress bacterial cell proliferation by blocking essential enzymes of microbial metabolism such as the proteolytic macerating enzymes. Saponins might act by altering the permeability of cell walls and hence exert toxicity on all organized tissues. They exert some antibacterial activity by combining with cell membranes to elicit changes in cell morphology leading to cell lysis [9]. It was suggested that polyphenols such as gallic acids act possibly by binding to bacterial dihydrofolate reductase (DHFR) enzymes, inhibition of supercoiling activity of *E.coli* bacterial gyrase by binding to the ATP binding site of gyrase B and binds to bacterial DNA thereby inducing topoisomerase IVenzyme-mediated DNA cleavage and bacterial growthstasis [2, 10].

Antioxidants protect cells against the damaging effects of reactive oxygen species otherwise called, free radicals such as singlet oxygen, super oxide, peroxyl radicals, hydroxyl radicals and peroxynite which results in oxidative stress leading to cellular damage [11]. Antioxidants exert their activity by scavenging the 'free-oxygen radicals' thereby giving rise to a fairly 'stable radical'. The free radicals are metastable chemical species, which tend to trap electrons from the molecules in the immediate surroundings. Free radicals generated in the body can be removed by the body's own natural antioxidant defences such as glutathione or catalases [12]. Therefore this deficiency had to be compensated by making use of natural exogenous antioxidants, such as vitamin C, vitaminE, flavones, beta-carotene and natural products in plants [13-15].

Plants contain a wide variety of free radicals scavenging molecules including phenols, flavonoids, vitamins, terpenoids hat are rich in antioxidant activity [13, 16]. Many plants, citrus fruits and leafy vegetables are the source of ascorbic acid, vitamin E, caratenoids, flavanols and phenolics which possess the ability to scavenge the free radicals in human body. Significant antioxidant properties have been recorded in phytochemicals that are necessary

for the reduction in the occurrence of many diseases [17, 18].

Many dietary polyphenolic constituents derived from plants are more effective antioxidants *in vitro* than vitamins E or C, and thus might contribute significantly to protective effects *in vivo*. Since free radicals are involved in a number of diseases such as gastrointestinal ulcerogenesis, the use of plants with antoxidant properties would reduce the incidence of enteric disorders [19].

Phytoconstituents employed by plants to protect them against pathogenic insects, bacteria, fungi or protozoa have been of relevance in human medicine [20].

Some phytochemicals such as phenolic acids act essentially by aiding in the reduction of particular adherence of organisms to the cells lining the bladder, and the teeth, which ultimately lowers the incidence of urinary tract infections and the usual dental caries.

Plants' volatile oils can also exert either bacteriostatic or bactericidal activity on microbes. The volatile gas phase of combinations of *Cinnamon* oil and clove oil showed good potential to inhibit growth of food spoilage organisms such as fungi, yeast and bacteria in the presence of high concentration of CO_2 and low concentration of O_2.

Many plants extracts have been shown to inhibit both the growth of *H*. *pylori in-vitro* as well as its urease activity. The efficiency of some extracts in liquid medium and at low pH levels enhances their potency even in the human stomach. Their inhibitory effect on the intestinal and kidney Na+/K+ ATPase activity and on alanine transport in rat jejunum has also been reported [21].

Phytochemicals such as epigallocatechin-3-gallate obtained from green tea have elicited inhibitory effects on the extracellular release of a toxigenic substance from *E. coli,* called verotoxin. Ethanol pericarp extracts from *Punica granatum* was also reported to inhibited verotoxin production in the periplasmic and cellular supernatant fluids. Although mechanisms by which phytochemicals elicit these actions are unclear, it is suggested that the active principles from these plants interfere with the transcriptional and translational processes ofthe bacterial cellular membranes [22]. Phytochemicals may also modulate transcription factors, redox-sensitive transcription factors, and redox signaling [23].

Clinical microbiologists have two reasons to be interested in the topic of antimicrobial plant extracts. First, it is verylikely that these phytochemicals will find their way into the arsenal of antimicrobial drugs prescribed by physicians. Examples of these are the bacteriostatic and antifugicidal properties of *Lichens,* the antibiotic action of allinine in *Allium sativum* (garlic), or the antimicrobial action berberines in golden seal (*Hydrastisca nadensis*).

All plants containing active compounds are important. The beneficial medicinal effects of plant materials typically result from the combinations of secondary products present in the plant. In plants, these compounds are mostly secondary metabolites such as alkaloids, steroids, tannins, and phenol compounds, which are synthesized and deposited in specific parts or in all parts of the plant. These compounds are more complex and specific and are found in certain taxa such as family, genus and species, but heterogeneity of secondary compounds is found in wild species.

The plants secondary products may exert their action by resembling endogenous ligands, hormones, metabolites, signal transduction molecules or neurotransmitters and thus have beneficial medicinal effects on humans due to their potential target sites similarities. Therefore, random screening of plants for active chemicals is as important as the screening of ethnobotanically targeted species.

Some of the simplest bioactive phytochemicals consist of a single substituted phenolic ring. Cinnamic and caffeic acids are common

representatives of a wide group of phenyl propane-derived compounds which are in the highest oxidation state. Some herbs such as tarragon and thyme both contain caffeic acid, which is effective against viruses, bacteria, and fungi. Catechol and pyrogallol both are hydroxylated phenols, shown to be toxic to microorganisms. Catechol has two hydroxyl groups, and pyrogallol has three. The site(s) and number of hydroxyl groups on the phenol group are thought to contribute to their microbial toxicity, with evidence that increased hydroxylation results in increased toxicity.

Quinones are aromatic rings with two ketone substitutions. They are ubiquitous in nature and are characteristically highly reactive. These compounds, being colored, are responsible for the browning reaction in cut fruits and vegetables and are an intermediate in the melanin synthesis pathway in human skin.In addition to providing a source of stable free radicals, quinones are known to complex irreversibly with nucleophilic amino acids in proteins, thereby resulting to the inactivation of the protein and loss of cellular function. For that reason, thepotential range of quinone antimicrobial effects is great. Probable targets in the microbial cell are surface-exposedadhesins, cell wall polypeptides, and membrane-bound enzymes. Quinones may also render substrates unavailable to the microorganism. Kazmi described an anthraquinone from *Cassia italica*, which inhibits *Bacillus anthracis*, *Corynebacterium pseudodiphthericum*, and *Pseudomonas aeruginosa* and bactericidal for *Pseudomonas pseudomalliae*. Hypericin, an anthraquinone from *Hypericum perforatum*, had been shown to possess antimicrobial properties [24].

Flavones are hydroxylated phenolic structures containing one carbonyl group which occur as a C6-C3 unit linked to an aromatic ring. They are synthesized by plants in response to microbial infection and they have been found to produce *in vitro* antimicrobial action against wide range enteric pathogens. Their activity is probably due to their ability to form complexes with extracellular and soluble proteins as well as the complexation with bacterial cell walls, thereby inducing microbial cell membrane perturbations [9].

Catechins are flavonoids that have been extensively researched due to their relative abundance in green teas. Flavonoid compounds exhibit inhibitory effects against bacterial strains such as *Vibrio cholerae*, *Streptococcus mutans*, *Shigella*, and some viruses.

Tannins are polymeric phenolic substances capable of precipitating gelatinous compounds from solution. Many human physiological activities, such as stimulation of phagocytic cells, host-mediated tumor activity, and a wide range of anti-infective actions, have been assigned to tannins. Thus, their mode of antimicrobial action, as described in the section on quinones may be related to their ability to inactivate microbial adhesins, enzymes, cell envelope transport proteins, etc. The antimicrobial significance of this particular activity has not been explored. The antimicrobial properties of tannins have been reviewed. From these studies, tannins were shown to be toxic to filamentous fungi, yeasts, and bacteria. Condensed tannins have been demonstrated to bind cell walls of ruminal bacteria, thereby inducing bacterial stasis and protease activity [25].

Several coumarins have demonstrated antimicrobial properties. R. D. Thornes, working at the Boston Lying-In Hospital in 1954, sought an agent to treat vaginal candidiasis in his pregnant patients. Coumarin was found *in vitro* to inhibit *Candida albicans*. Hydroxylated derivatives of coumarins such as phytoalexins, are produced in carrots in response to fungal infection and it is presumed to elicit antifungal property. General antimicrobial activity was documented in woodruff (*Galium odoratum*) extracts [26].

Terpenenes or terpenoids are active against bacteria, fungi, viruses, and protozoa. In 1977, it was reported that 60% of essential oil derivatives

examined to date were inhibitory to fungi while 30% inhibited bacteria. The ethanol-soluble fraction of purple prairie clover yields a

terpenoid called petalostemumol, which showed excellent activity against *Bacillus subtilis* and *Staphylococcus aureus* and lesser activity against gram-negative bacteria as well as *Candida albicans*. Two diterpenes isolated by Batista *et al.,*[27], were found to inhibit *Staphylococcus aureus*, *V. cholerae*, *P. aeruginosa*, and *Candida* spp.

The inhibition of bacteria and fungi by lectins, such as those from the herbaceous *Amaranthus spp*, had been documented. Thionins found in barley and wheat and consist of 47 amino acid residues have shown significant toxicity to yeasts, gram-negative as well as gram-positive bacteria [28]. Fabatin, a newly identified 47- residue peptide from fava beans, had demonstrated some activity against some enteric pathogens such as *E. coli*, *P. aeruginosa*, and *Enterococcus hirae.* Generally, they are extremely toxic though they do have a marked therapeutic effect in minute quantities. For this reason, plants containing alkaloids were not often used in folk medicine and then for external application only. Pure, isolated plant alkaloids and their synthetic analogues were used as analgesics, antispasmodics, and bacterial chemotherapeutic regimes [29].

The reports of antimicrobial properties associated with polyamines, isothiocyanates, thiosulfinates and glucosides, deserve special mention. The antimicrobial effects of cranberry juice have been documented. In ancient times, women have been told to drink he juice in order to prevent and even cure urinary tract infections. In the early 1990s, studies revealed that the monosaccharide fructose present in cranberry and blueberry juices competitively inhibited the adsorption of pathogenic *E.coli* to urinary tract epithelial cells, acting as an analogue for mannose. Clinical studies have borne out the protective effects of cranberry juice. Many fruits contain fructose, however, and researchers are now seeking a second active compound from cranberry juice which contributes to the antimicrobial properties of this juice [30].

CONCLUSION

The mechanisms of antimicrobial action of plant-derived principles against enteropathogenic microbes were investigated and the results obtained from the research carried out by Moyo *et al.* [9] portend that, plant-based antibiotics exhibit alternative mechanisms that would be of relevance for the prophylaxis and chemotherapy of gastrointestinal infections that are becoming refractory to the current arsenal of the previously susceptible allopathic antibiotics. Although this is a preliminary research, it is suggested that the molecular basis for the modes of action of plant-based antibiotics be ascertained and determine if these phytochemicals would exhibit these mechanisms *in vitro* on sensitive enteric pathogenic microorganisms.

REFERENCES

1. Xavier D et *al*. Microevolutionary Analysis of *Clostridium difficile* Genomes to Investigate Transmission. Genome Biology: [cited 2014 March 27]. Available from: *http://genomebiology.com/2013/12/12/R118.*
2. Enwa FO, CG Omojate and C Adonu. A Review on the phytochemical profile and the antibacterial susceptibility pattern of some clinical isolates to the ethanolic leaves extract of *Moringaoleifera* lam (moringaceae). International Journal of Advanced Research 2013; 1 (5): 226-238.
3. Kar A. Pharmaocgnosy and Pharmaco-biotechnology. New Delhi: New Age International Limited Publishers; 2007, p 332.
4. Kris-Etherton PM et al. Bioactive compounds in foods: their role in the prevention of cardiovascular disease and cancer. American Journal of Medicine 2002; 113:715-885.

5. Manson, M.M. Cancer prevention – the potential for diet to modulate molecular signalling. Trends in Molecular Medicine. 2003; 9: 11–18.
6. Surh YJ. Cancer chemoprevention with dietary phytochemicals. Natural Reviews in Cancer 2003; 3: 768–780.
7. Kotzekidou P, Giannakidis P and Boulamatsis A. Antimicrobial activity of some plant extracts and essential oils against foodborne pathogens in vitro and on the fate of inoculated pathogens in chocolate. LWT - Food Science and Technology *2008; 41(1):119-127.*
8. Onyekaba TU, Omojate CG and Anowi FC. Phytochemical screening and investigations of antibacterial activities of various fractions of the ethanol leaves extract of *Moringa oleifera* lam (Moringaceae). International Journal of Pharmaceutical, Chemical and Biological Sciences 2013; 3 (3): 962-973.
9. Moyo et al. Antimicrobial activities of *Moringa oleifera* lam extracts. African Journal of Biotechnology 2012; 12:34-42.
10. Sakharkar M K *et al*. Activity and interactions of antibiotic and phytochemical combinations against *P.aeruginosa* in vitro. International Journal of Biological Science 2010; 6(6):556-568.
11. Mattson MP and Cheng A. Neurohormetic phytochemicals: low dose toxins that induce adaptive neuronal stress responses. Trends in Neurosciences 2006; 29(11): 632-639.
12. Madsen H L and Bertelsen G. Spices as antioxidants. Trends Food Science and Technology 1995; 6: 271-277.
13. Rice-Evans C, Miller N and Paganga G. Antioxidant properties of phenolic compounds. Trends in Plant Science 1997; 2: 152-159.
14. Diplock AT et al. Functional food science and defence against reactive oxidative species. Brazilian Journal of Nutrition 1998; 80: 77-112.
15. Cai YZ and Sun M. Antioxidant activity of betalins from plants of the Amaranthacea. Journal of Agriculture and Food Chemistry 2003; 51: 2288-2294.
16. Hertog MGL and Feskens EJM. Dietary antioxidant flavonoids and risk of coronary heart disease: the zutphen elderly study. Lancet 1993; 342: 1007-1011.
17. Anderson KJ and Teuber SS. Walnut polyphenolics inhibit *in vitro* human plasma and LDL oxidation, biochemical and molecular action of nutrients. Journal of Nutrition 2001; 131: 2837-2842.
18. Jayasri MA, Mathew L and Radha A. A report on the antioxidant activities of leaves and rhizomes of *Costus pictus D*. *Don*. International Journal of Integrative Biology 2009; 5(1):20-26.
19. Nascimento GGF et al. Antibacterial activity of plant extracts and phytochemicals on antibiotic-resistant bacteria. Brazilian Journal of Microbiology 2003; 1:247-256.
20. Jakhetia V et al. Cinnamon: A pharmacological review. Journal of Advanced Scientific Research 2010; 1(2): 19- 23.
21. Voravuthikunchai SP and Kitpipit L. Activities of crude extracts of thai medicinal plants on methicillin- resistant S*taphylococcus aureus.* Journal of Clinical Microbiology and Infection 2003; 9:236- 240.
22. Andreadi CK et al. Involvement of Nrf2, P38, B-Raf, and nuclear factor-Kappab, but not phosphatidylinositol 3- kinase, in induction of hemeoxygenase-1 by dietary polyphenols. Molecular Pharmacology 2006; 69:1033–1040.
23. Trease G and Evans W. Pharmacognosy, Aberdeen, Great Britain: Univ. Press; 1972.
24. Kazmi MH et al. An anthraquinone derivative from Cassiaitalica. Phytochemistry 1994; 36: 761–763.
25. Jones GA et al. Effects of sainfoin (Onobrychis viciifolia scop.) condensed tannins on growth and proteolysis by four strains of ruminal bacteria. Applied Environmental Microbiology 1994; 60:1374–1375.

26. Thomson WAR (Ed.). *Medicines from the Earth*. United Kingdom: Mcgraw-Hill Book Co.; 1978, p 55.
27. Batista O et al. Structure and antimicrobial activity of diterpenes from the roots of Plectranthus hereroensis. Journal of Natural Products 1994; 57:858–861.
28. Fernandez de Caleya R et al. Susceptibility of phytopathogenic bacteria to wheat purothionins in vitro. Applied Microbiology 1972; 23(5):998–1000.
29. Stary F. The natural guide to medicinal herbs and plants. New York: Barnes & Noble Inc.; 1996.
30. Zafriri D et al. Inhibitory activity of cranberry juice on adherence of type 1 and type P fimbriated *Escherichia coli* to eucaryotic cells. Antimicrobial Agents & Chemotherapy 1989; 33(1):92–98.

Cite this article as:
Omojate Godstime C, Enwa Felix O, Jewo Augustina O and Eze Christopher O. Mechanisms of antimicrobial actions of phytochemicals against enteric pathogens – a review. J Pharm Chem Biol Sci 2014; 2(2):77-85.