AkiNik

International Journal of Herbal Medicine
Available online at www.florajournal.com

I J H M International Journal of Herbal Medicine

ISSN 2321-2187
IJHM 2013; 1 (4): 102-106

Received: 11-09-2013
Accepted: 19-11-2013

Omari Amuka
Department of Applied Plant Sciences, Maseno University, Private Bag, Maseno, Kenya.

Paul Okemo
Department of Plant and Microbial Sciences and [3] Department of Chemistry Kenyatta University, P.O. Box 43844, Nairobi, Kenya

Alex Machocho
Department Chemistry Kenyatta University, P.O. Box 43844, Nairobi, Kenya

Paul Mbugua
Department of Plant Sciences and Kenyatta University, P.O. Box 43844, Nairobi, Kenya

Eliud NM Njagi
Department of Biochemistry and Biotechnology, Kenyatta University, P.O. Box 43844, Nairobi, Kenya

Anthony Nyamache
Department of Plant and Microbial Sciences and Department of Chemistry Kenyatta University, P.O. Box 43844, Nairobi, Kenya

Correspondence:
Omari Amuka
Department of Applied Plant Sciences, Maseno University, Private Bag, Maseno, Kenya.
Email: oamuka@maseno.ac.ke

Intercession of Phytomedicine in the Challenges of Emerging, Re-Emerging Diseases; and Pathogens Resistance to Antibiotics

Omari Amuka, Paul Okemo, Alex Machocho, Paul Mbugua Eliud NM Njagi and Anthony Nyamache

Abstract
The review higlights the accelerated rate at which pathogens are developing resistace to known antibiotics that are currently in use. The emergence of new maladies and reemergence of old ones has been highlighted. The role played by plants in tackling the challenges has been emphasized. The approach taken is based on the geographical location of various civilizations in which the plants are/were used as a source of remedies throughout the five continents of the world. Globally, there is a trend of erratic antibiotic use this which has led to challenges of their regimen. This has resulted in the influx of increased. There is also an urgent need for patient education on the use of such drugs. There is also emergence and reemergence of new new maladies. The only answer to such challenges is found in phytomedicine.

Keywords: Antibiotics; Re-Emerging Diseases; Pathogens Resistance.

1. Erratic use of antibiotics

Globally, drug abuse by users has reached arming levels to the authorities. For example, in Croatia, in one of the teaching hospitals showed that tight control of antibiotics was necessary [1]. Antibacterials were evaluated in two years and it emerged that the antimicrobial utilization was similar in both years. However, the pattern of utilization had changed in contrast to the outpatient setting where the pattern of antimicrobial prescription remained the same. There was more liberal prescription of over the counter access as compared to the previous years when certain drugs were restricted [1]. Furthermore, it established the fact that when the use of antibiotics is controlled, there is likelihood that the bacteria do not develop resistance to the antibiotics used. Common typhoid fever is generally caused by *Salmonella enterica serovar. Typhirunium* (common name S. *typhi*.) are Gram-negative and their treatments are difficult [2]. The antibiotics used in the management of the diseases include chloramphenical as the first drug of choice. Other drugs which may be employed are ampicillin, penicillin G, Norfloxacin, Streptomycin and Rifampicin. However, there are cases of resistances to antibiotics which were later traced to genetic changes within the cell structure [3]. This was noticed when certain strains were subjected to fusidic acid which is a steroid like antibiotic and which establishes EF-G. GDP on the ribosome after translocation has occurred thereby blocking protein synthesis. Against this backdrop of genetic modifications, phenotypes of the organism with variable susceptibility to the mentioned antibiotics have emerged. Nosocomial systemic bacterial infections have revealed that there is a correlation between nosocomial infections and mortality. Such mortalities have been further complicated by the fact that pathogens so studied have strains that are resistant to treatment by more conventional or the *β lactam* antibiotics [4]. The research was carried out on strains of both Gram-positive and Gram-negative bacteria which included *Staphylococcus, E. coli, Klebsiella* spp, *Enterobacter* spp., *Serretia* spp and other Gram- negative Bacilli. It was evident that Methicillin resistant strains of Staphylococci and penicillin G resistant Streptococci, ampicillin resistant enterococci and cefotaxime resistant enterobacteriaceae *Pseudomonas* spp. were resistant to the drugs that were currently in use in hospital. The above data provided hospital decision makers with pertinent information on the clinical consequences of nosocomial infections caused by antibiotic resistant bacteria.

It is important to mention that there are possibilities of Universal bacterial attacks as epidemics. In the 21st century, affluent societies lived under the impression that they were free from attack of pathogenic bacteria and if they suffer by accident, there would be an antibiotic to cure the malady [5]. This is false and it is prognosed that if the conditions of discovering new drugs remain (status quo) the fatalities from such cases may be alarming. The impression that the antibiotics are available within short notice to combat diseases is a fallacy and such a notion may consequently result into a catastrophic event [6]. This is so because antibiotics have kept human and livestock from many plagues that constituted scourges of humanity until the second half of the 20th century. Ironically antibiotics are weak marketable goods in that patients stop buying them once they recover, after short courses of treatment before the completion of the stipulated period of treatment [7]. To date, a vast majority of infections caused by *Staphylococcus aureus* are penicillin resistant [8]. Hitherto, new ones only provide short respite until new resistance emerges which are staphylococcal based. For example bovine mastitis infection induced by *S. aureus* difficult to eradicate by conventional antimicrobial therapies [9]. *In vivo* studies in mice indicated that the pathogens persisted in mice despite being treated with antibiotics. Such studies were conducted using several mutants of the bacteria which included isogenic hem mutants that had small colony variant (scv) phenotype. The latter mutant expressed a marked inability to colonise tissues. Although the hem mutant and *S. aureus* were susceptible *in vitro* to cephapirin, it was 100 times more persistent than the parental strains in the mammary glands when the antibiotics were administered at the rate of 1 or 2 mg/ kg [9]. The studies concluded that despite the fact that hem. B mutant has reduced ability to colonise mammary glands, scv phenotype may account for the persistence of *S. aureus* under antibiotic *in vitro*. Although it may seem obvious, it is essential to point out that the antibiotics that were easy to discover have already been found but, the search for new ones involves a substantial amount of high quality and laborious research [10]. Currently, there are various antibiotics which can combat most bacterial diseases but several alarms have been raised to develop new antimicrobials which could be used to combat the newly emerging resistant ones [11]. The need has been prompted by several reasons, which includes the spread of multi-drug resistant organisms, the spread of emerging and re-emerging pathogens and the consequential high social and economic impacts of infectious diseases. Although vaccinations are a classical way of controlling infections, they can only be used for preventive and not curative measured once the disease is established [12] [12]. Vaccines such as the pneumococcal one may also help in the reduction of antibiotic resistant isolates. However, there have been controversies since studies have failed to establish the role of vaccination in the reduction of resistance but have suggested that reduction of antibiotic pressure may be needed to reduce the frequency of resistance [13]. Research may also be slowed down because of the attitude of the clinicians who are satisfied by the fact that what they have is good enough for the time being. The belief that the need for new antibiotics is not pressing may then appear as justified. However, for cases involving elderly or immunocompromised patients, for whom the prognosis is so dangerously poor, the development of new treatment should be a matter of priority. Patients with diverse medical conditions including those immunocompromised are in one way or the other likely to create another segment with the risk of succumbing to infections in any given human populations. In developed countries, nosocomial infections occur in 5-7% of patients hospitalized for other reasons, hence an is increase in hospital stay for at least an average time of four extra days, which increases the cost of hospitalization by U$500 [12] and [14]. It is more complicated when the patients are in the intensive care unit in that both the risk and the cost are more than doubled; their additional stay can extend up to nineteen days with a concomitant higher mortality rate, often associated with antibacterial therapeutic failure [15].

2. Mortalities from antimicrobials

The literature hinted that bacterial infectious diseases have impacts with far-reaching effects in terms of morbidity and mortality. In developing countries alone, according to the [16], statistics, on bacteria and bacterial related infections are responsible for 60% of the annual mortality. Amongst the malnourished and elderly, despite existing antibiotic therapies and vaccine, bacteria remain the leading source of morbidity and mortality rest of the world [17]. Pathogens also contribute to a third of the deaths and ailments both in Europe and worldwide. Although vaccination contributes substantively towards curbing pneumonia, it does not provide full protection because not all individuals respond equally well to the immunization and because the immunity provided by the available capsular polysaccharide based vaccines do not cover all the possible serotype variants of the pathogen [18]. It would be imperative to look for therapeutic techniques that seek to minimize accelerated development of resistance by micro-organisms to antibiotics; there has been marginal impact of patient education on antibiotics prescribed to children with pharyngitis and adults with acute bronchitis in private practices [19]. Profiling the physicians' prescription, records revealed that there was increase in antibiotic prescription for children with pharyngitis in distant control but decrease in local control practices and intervention cases had the highest decrease from 34 to 30%. In adults control through education reduced substantively from 55 to 44% in local control, from 50 to 44% in distant control, and from 60 to 36% at the intervention practices.

3. Patient education on drug abuse

Patient education can help to reduce antibiotic use for adults through physician directed efforts and restrictions. The foregoing statement has more to do with ethical perspective as opposed to the open happy physicians who prescribe antibiotics at the mention of ailment without carrying out diagnostic survey and investigations [20]. With the unending problems with antibiotics, the studies for alternatives are necessary to evolve potent antibiotics with unending problems with antibiotics, the studies for alternatives are necessary to evolve potent antibiotics with activities against both Gram-positive and Gram-negative bacteria. Antibiotic activities of the extracts from the study of plants were comparable to the standard antibiotics with a zone of inhibition seen to be quite potent [21]. Local communities in Western Kenya claim that there are certain plant extracts, which are known to have antibiotic activities and such plants include: *Chamaecrista*

abrus against measles, *Emilia cocnea* against syphilis and *Philiostigma thoningii* against gonorrhoea [22]. Some plants like *Kedrostis foedisima* and *Melia Azadiracta* are used for the treatment of general viral rashes and swellings like measles and mumps. *Aloe* ssp. is used for treatment of herpes zoestra.

4. Remedy from plants against viral infections

Currently, tackling "modern" emerging infections is crucial [23]. For instance an increasing number of HIV infections and AIDS cannot use the currently approved anti HIV drugs, including the reverse transcriptase and protease inhibitors due to the adverse effects and the emergence of drug resistance [24]. Many of the antivirals presently in use have narrow spectrum activity and restricted therapeutic usefulness [25]. Despite the fact that most governments provide free ARVs, it is still not yet 100% coverage among patients in need of antiretroviral drugs. These drugs are expensive and beyond the reach for most of the victims. For the last two decades, scientists have been forced to address the epidemic, which has drastically retarded socio-economic development and in turn resulted in a wildfire rate of its spread.

There are other plant species, which yield similar compounds with the same activities [26]. Such species are from the Euphorbiaceae family which include plants like *Euphorbia poissonii*; some plants with anticancer principles like *Pedilanthus* ssp. and showed activities against HIV–1 Virus [27]. Oleanolic acid was also identified as an anti HIV principle from several plants, which include *Rosa woodsii*, leaves, *Hyptis capitata* (whole plant) *Syzigium clariflorum* leaves and *Terenstromia gymnathera*. There are also other classes of compounds from plants, which have useful effects against the HIV virus [27] which include alkaloids, proteins, polypheriols and polysaccharides. There are also other plant extracts, though unclassified, that have been found to have antiviral activities. The plant extracts, however, have been studied *in vivo* and *in vitro* animal experimental models. However, no clinical trials have been conducted yet. Apart from malaria, AIDS is the leading infectious cause of death in the world. Untreated disease caused by HIV has a fatality rate of 100%. Nevertheless, it should be stressed that a number of natural products mainly derived from plants have proved effective in suppressing HIV replication and progress [28]. In regions where herbal medicine could be considered to be at par with the current dominant allopathic medicine, most of the therapeutic plants are from the traditional data bank [23]. Several plants were investigated to establish their scientific potential values in the management of HIV. It emerged that quite a considerable number had antiretroviral activities and potential drug development that are comparable to the drugs currently in the market [23]. This revelation enhances the use and encourages further studies on the use of plants in tackling modern problems and conservation of indigenous knowledge in Africa. However, only a meagre portion of East African plants has been currently covered in the ongoing work *in vitro* as in the case of [29] on trying to find out new antiplasmodia compounds from the indigenous flora from the East African region.

5. Emerging and remerging diseases; a burning issue

Problems of emerging and reemerging resistant micro-organisms and their strains are common phenomena [30]. The contious development of antimicrobial resistance to the drugs currently used has called for an urgent attention for development of novel drugs. Some of the organisms that were previously easily managed by use of common antibiotics have become a challenge in patients' management. For instance, *E. coli*, under virulent conditions, causes extra intestinal infections a wide diverse spectrum of diseases including: urinary tract infections and (UTI), new born meningitis, abdominal sepsis and septicemia [30]. All these infectious diseases have posed a challenge on their management due to high incidence rates of drug resistance being transmitted by plasmids [19, 31]. Studies have shown that antibiotics can start to lose their efficacy at the beginning of their clinical use through the development of antibiotic resistance by bacterial pathogens [32]. The emergence of antimicrobial resistance is primarily due to excessive and often unnecessary use of antibiotics in humans and animals [33, 34]. Use of counterfeit drugs and suboptimal management of drugs due to lack of education are some of the factors associated with development of antibiotic resistance. Challenges in antimicrobial resistance are more real due to emerging and reemerging diseases. The advent of HIV/AIDS epidemic have also led to over use of drugs like Trimethoprime-Sulfisoxazole for the prevention of opportunistic infections. This overuse propagates antibiotic resistance. In addition, HIV infection is associated with primary multi-drug resistant-tuberculosis [34, 35]. Challenges in antimicrobial resistance are more real due to emerging and reemerging diseases. It is, therefore, empirical that further studies on antibiotic discovery is vital considering the threat posed by the emergence of drug resistance [35]. The best example is the frequent upsurge of Legionella, an organism which becomes a threat due to change of lifestyle of using air conditioning systems more frequently. Such a condition enhances quick multiplication of the organism and its delivery to the human respiratory system. Based on metagenomics in microbiology, it is possible to identify the gene pool which is either cultivable or not cultivable which may be used in future identification of unexpected potential pathogens following the identification of all the virulence related genes–"resistone" present in the environment [37]. The ecological impact of human activity is well-illustrated by the changes seen in antibiotic resistance through the years [38]. Bacteria quickly develop resistance to antibiotics usually within a few years of their commercial manufacture and marketing. For example, in 1943, when penicillin was first prescribed, virtually all Gram-positive infections were susceptible to its effects on cell wall synthesis [38]. However, the bacteria soon developed resistance to the drug and by 1946, resistant strains were already well-recognized. Mycobacteria require special attention, but lightly, because it causes infections of a killer disease, tuberculosis (TB). Currently, the disease is the leading cause of death worldwide from a single human pathogen. The disease claims more adult lives and children than diseases like AIDS, malaria, diarrhoea, leprosy and all the other tropical diseases combined (3S, 4R). It is estimated that a third of the world's population is currently infected with *M. tuberculosis*, where 10% of those infected will develop clinical diseases, more so those that are immunosuppressed or immunocompromised as a result of HIV (3S, 4R). Although there are several broad spectrum antibiotics, there has been an upsurge in the mortality rate due to the emergence of multi drug resistant strains of *M.*

tuberculosis [39]. By the year 2000 the mortality due to the disease had reached over 3.5 million [40, 41]. The upsurge in the incidences of TB mortality is further attributed to poor physical infrastructure in the rural areas where majority of the developing world live, lack of diagnosis and drug supply. There is also poor supervision and medical care and as a result of which drug resistance develops [10]. This means that there is need for broad spectrum effective treatment to curb this malady. Tuberculosis was considered as a conquered malady that was disappearing, but has made a comeback in the recent past [41]. This new scenario is not only due to the association of *Mycobacterium* with AIDS but also due to evolution of strains of the pathogens that are resistant to several drugs which are currently in use [41]. It seems clear that besides biomedical research, additional social measurements are urgently needed to deal with the problem of infectious diseases in a global scenario.

6. Conclusion

With all the above surveyed and discussed scenarios, it would be logical to do a documentation of the local medicinal flora for future references. It is also imperative that a thorough pharmacological profiling be done if a scientific selection and discovery of the new products is to be achieved. Finally, it is important that; the pharmcognosy of such drugs is carried out to assist in the selection of the new products for commercial development. Such are the compounds that may be used to intervene in the eradication of the rapidly mutating pathogens.

7. Reference

1. Palcevski VV, Francetic I, Palcerski G, Bazijanac V R. Utilization of antimicrobials in Rijeska Croatia. J of Pharmacoepidemiology and Drug Safety 2004; 13: 105-110
2. Macvanin M, Hughes D. Hyper- susceptibility of a fusidic acid resistant mutant of *Salmonella* spp to different classes of antibiotics. FEMS Microbiology Letters 2005; 247:215-220.
3. Guillemot D, Gasquent I, Valet O, David MF, Laurent C, Mathieu D. Thirty day mortality of nosocomial systemic bacterial infections according to antibiotic susceptibility in an 800- bed teaching hospital in France. J of Clinical and Microbiol Infection 2005; 2:502-504.
4. Machado TB, Leal ICR, Kuster RM, Amaral ACF, Kokis V, Silva MG *et al*. Brazilian Phytochemicals - Evaluation against Hospital Bacteria. Phytotherapy Research 2005; 19:519-525.
5. Vicente M, Hodgson J, Massida O, Tonjum T, Henriques-Normark B, Ron EZ. The Fallacies of Hope: Will We Discover New Antibiotics to Combat Pathogenic Bacteria in Time. FEMS Microbiology Review 2006; 000-0021.
6. Palumbi SR, Humans as. The world's greatest evolutionary force. *Science* 2001; 293: 1786-1790.
7. Brouillette E, Martines A, Boyll B J, Allen NE, Malouin F. Persistence of *Staphylococcus aureus* small colony variants under antibiotic pressure *in vivo FEMS Immunology and Medical Microbiology* 2004; 41: 35-41.
8. Ernst E. The efficacy of herbal medicine – an overview. J of Fundamental and Clinical pharmacology 2005; 19:405-409.
9. Seguin P, Laviolle B, Chanavaz C, Donnio PY, Gautier-Lerestif AL. Factors associated with multidrug-resistance bacteria in secondary peritonitis Impact on antibiotic therapy. J of Clinical Microbiology and Infection 2006.
10. Webster DE, Thomas MC, Pickering R, Whyte A, Dry IB. Is there a role for plant-made vaccines in the prevention of HIV/AIDS. J of Immunology and Cell Biology 2005; 83:239-247
11. Frazao N, Brito–Avo A, Simas C. Effect of the seven-valent conjugate pneumococcal vaccine on carriage and drug resistance of *Streptococcus pneumoniae* in healthy children attending day care centers in Lisbon. J of Pediatric Infectious Diseases 2005; 24:243-252.
12. Sade P, Holtzer I, Levo Y, Kivity S. The economic burden of antibiotic treatment of penicillin-allergic patients in internal medicine wards of a general tertiary care hospital. CIM Exp Allergy 2003; 33: 501-506.
13. Howard DH. Resistance-Induced antibiotic substitution. J of Health Economics 2004; 13:585-595.
14. Kollerf H. The Importance of appropriate initial antibiotic therapy for hospital – acquired infections. American J.of Medicine 2003; 115:582-584
15. WHO. Technical Report Series Advances Malaria Chemotherapy. World Health Organization, Geneva, 1984; 711:91-100.
16. Mackenzie FM, Struelens MJ, Towner KJ, Gould IM. Report of the Consensus Conference on Antibiotic Resistance Prevention and Control. J of Clinical Microbiology and infection 2005; 11:11.
17. Ron EZ, Host specificity of *Escherichia coli*. Human and avian pathogens. Current Opinions in Microbiology 2006; 9:28-32.
18. Bernatoniene J, Finn A. Advances in *pneumococcal* vaccines advantages for infants and children. Drugs 2005; 65:229-255.
19. Gonzales R, Corbett KK, Lee-Castillo BA, Glazner J, Erbacher K, Dar CA. The "Minimizing Antibiotic Resistance in Colorado" Project Impact of Patient Education in Improving Antibiotic Use in Private Office Practices. HSR Health Services Research 2005; 40:1.
20. Barnes J. Quality efficacy and safety of complementary medicines fashions, facts and future. Part II Efficacy and Safety. British J. of Clinical Pharmacolology 2003; 55:331-340.
21. Chhabra SC, Mahunnah RLA, Mshui RLA. Plants used in traditional medicine in Eastern Tanzania – VI. Angiosperms (Sapotaceae to Zingiberaceae). J of Ethnophamacology 1993; 39:83-103.
22. Kokwaro JO. Medicinal Plants of East Africa. E.A. Literature Bureau 1993; 116-120.
23. Li Y Ooi, S. ML, Wang H, But PPH, Ooi VEC. Antiviral Activities of Medicinal Herbs Traditionally Used in Southern China Mainland. Phytotherapy Research 2004; 18:718-722.

24. Thumbran S, Klaesen J, Mabusela WT, Cannon JF, Folk W, Johnson Q. T*ulbaghia alliacea* Phytotherapy A potential anti-infective remedy for candidiasis. Phytotherapy Research 2006; *DOI: 10 1002/ptr*. 1945.
25. Asres K, Seyoum A, Veeresham C, Bucar F, Gibbon S. Naturally Derived Anti-HIV Agents. Phytotherapy Research 2005; 19:557-581.
26. Akiyemi K O, Oladapo O, Okwara C, Ibe ECC, Fasure KA. Screening of crude extracts of six medicinal plants used in South West Nigeria Unorthodox medicine for anti-methicillin resistant. Staphylococcus aureus BMC Complementary and Alternative Medicine 2005 5: 6 doi: 10. 1186/1472-688 2–5- 6.
27. Petit GR, Ducki S, Tan R. Isolation and structure of pedistatin from a Republic of Maldives (*Pedilanthus* sp). J of Natural Products 2002; 65:1262-1265.
28. Ron EZ. Host specificity of *Escherichia coli* Human and avian pathogens. Current Opinions in Microbiology 2006; 9:28-32.
29. Garau J. Impact of antibiotic restrictions the ethical perspective. J of Clinical Microbiology and Infection 2006; 12:16-24.
30. Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases. Nature 2004; 430:242-249.
31. D'Costa VM, McGrann KM, Hughes DW, Whight GD. Sampling the antibiotic resitome. *Science* 2006; 311:374-377.
32. Marrie TJ. Therapeutic implications of macrolida resistance in *Pneumococcal* community acquired lower respiratory tract infections. International J. Clinical Practices 2004; 58(8):769-776.
33. Zumla A, Grange J. Doing something about tuberculosis. Clinical Review Tuberculosis BMJ 1998; 16:1962–1964.
34. Rao GG. Risk factors for the spread of antibiotic-resistant bacteria. Drugs 1998; 55(3):323-30
35. WHO. Report of the Inter-regional workshop on Intellectual property right in the contexts. 1985.
36. Newton SM, Lau C, Wright CW. A Review of Antimycobacterial Natural Products. Phytotherapy Research 2000; 14:303-322.
37. WHO. Legal Status of Traditional Medicine, Complementary Alternative Medicine: a Worldwide Review. World Health Organization, Geneva. 2001.