Bima Journal of Science and Technology Vol. 2 No. 2 June, 2018 ISSN 25366041

EFFECT OF QUERCETIN AND ITS 7-METHOXY DERIVATIVE ON THE ANTIBACTERIAL ACTIVITY OF CIPROFLOXACIN IN SOME SELECTED BACTERIA

[1]Sada, H.,[1]Sallau, M. S, [2]Musa, A. M., [1]Habila, J. D.
[1]Department of Chemistry, Ahmadu Bello University, Zaria
[2]Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University, Zaria

Abstract

Infectious diseases account for approximately one-half of all deaths in tropical countries and the rate at which antibiotic resistant bacteria emerge is not matched by the rate of development of new antibiotics to combat them. Flavonoids is an important class of compounds with diverse biological activities which include interesting areas such as anti-oxidant, anti-aging, anti-cancer, anti-bacterial and anti-viral. The aim of this study is to determine the potential synergistic effect of Quercetin and 7-methoxyquercetin on antibacterial activity of Ciprofloxacin. Agar well diffusion method according to the National Committee for Clinical Laboratory Standard (NCLSI, 2011) was adopted for the study and organisms tested include: Vancomycin resistant *Staphylococcus aureus* (VRSA), methicillin resistant *Staphylococcus aureus* (MRSA*), Bacillus substilis*, *Salmonella typhi*, *Klebsiella pneumonia* and *Escherichia coli.*The compounds Quercetin and 7-methoxyquercetin potentiate the antimicrobial activity of 15 µg/ml ciprofloxacin (zone of inhibition ranging from 32-37 mm) as against ciprofloxacin (30 µg/ml) alone(zone of inhibition ranging from 30-32 mm).The above findings suggest that the compounds can be used to enhance the antibacterial activity of ciprofloxacin

Keywords: Antibacterial, synergy, Ciprofloxacin, Quercetin,7-methoxyquercetin.

Correspondence Author: sadahadiza@gmail.com, 08030707700.

Introduction

Infectious diseases account for approximately one-half of all deaths in tropical countries (Iwu, *et al.*, 1999). This may be due to poverty, increasing incidence of multiple drug resistance and side effects associated with currently available antimicrobials. The increasing phenomenon of acquisition of resistance among microorganisms to antimicrobial drugs is attributed to the indiscriminate and improper use of current antimicrobial drugs (Usha*et al.*, 2010).The rate of emergence of antibiotic resistant bacteria is not matched by the rate of development of new antibiotics to combat them (Prescott and Klein, 2002).The steadily increasing bacterial resistance to existing drugs is a serious problem, and therefore there is a dire need to search for new classes of antibacterial substances, especially from natural sources. Unlike synthetic drugs, antimicrobials of plant origin are not associated with side effects and have a great therapeutic potential to heal many infectious diseases (Chanda*et al.*, 2010; Habbal*et al.*, 2011). An

alternative therapy to treat antibiotic resistant microorganisms is the use of plant extracts. Drugs derived from natural sources play a significant role in the prevention and treatment of human diseases. There are several reports on the antimicrobial activity of different plant extracts that were effective antimicrobials (Vaghasiya*et al*., 2008; Fisgin*et al*., 2009; Jeong*et al*., 2009; Darwish and Aburjai, 2010; Yoon *et al*., 2011). There are many advantages of using antimicrobial compounds from medicinal plants, such as fewer side effects, better patient tolerance, less expensive, acceptance due to long history of use, and being renewable in nature (Gur*et al*., 2006) and also higher plants represent a potential source of novel antibiotic prototypes (Parekh and Chanda, 2007).

The need of the hour is to develop still newer, useful and important antimicrobial agents (Sharma and Kumar, 2006; Negi and Dave, 2010); or new ways to treat the resistant microorganisms. An alternative approach is the use of combination therapy i.e. synergism between known antibiotics and bioactive plant extracts or the bioactive compounds isolated from plants.

Flavonoids continue to capture the interest of scientists from different disciplines because of their structural diversity, biological and ecological significance (Williams and Grayer, 2004). Their diverse biological activities include interesting areas such as anti-oxidant, anti-aging, anti-cancer,anti-bacterial and anti-viral (Chen *et al.,* 2002).

In our previous work, we reported the isolation and characterization of the compounds (sada*et al.*, 2016). This study is aimed at investigating the effect of the compounds on the antibacterial activity of ciprofloxacin.

Methodology

Plant

The plant sample, *Globimetulaoreophila* was collected around Area BZ, Ahmadu Bello University, Zaria staff quarters. The plant was authenticated by NamadiSunusi of the Herbarium unit, Department of Biological Sciences, Ahmadu Bello University Zaria-Nigeria by comparing with an existing specimen with voucher number 2839. The plant material was air-dried and pulverised into powder using pestle and mortar.

Test Organisms

The microorganisms tested include Vancomycin resistant *Staphylococcus aureus* (VRSA), methicillin resistant *Staphylococcus aureus* (MRSA*), Bacillus substilis*, *Salmonella typhi*, *Klebsiella pneumonia* and *Escherichia coli.* Clinical isolates of the organisms were obtained from the Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University, Zaria, Nigeria.

Extraction

Polarity Based Extraction (PBE) method described by Harborne, 1983 was adopted with some modification (Figure 1).

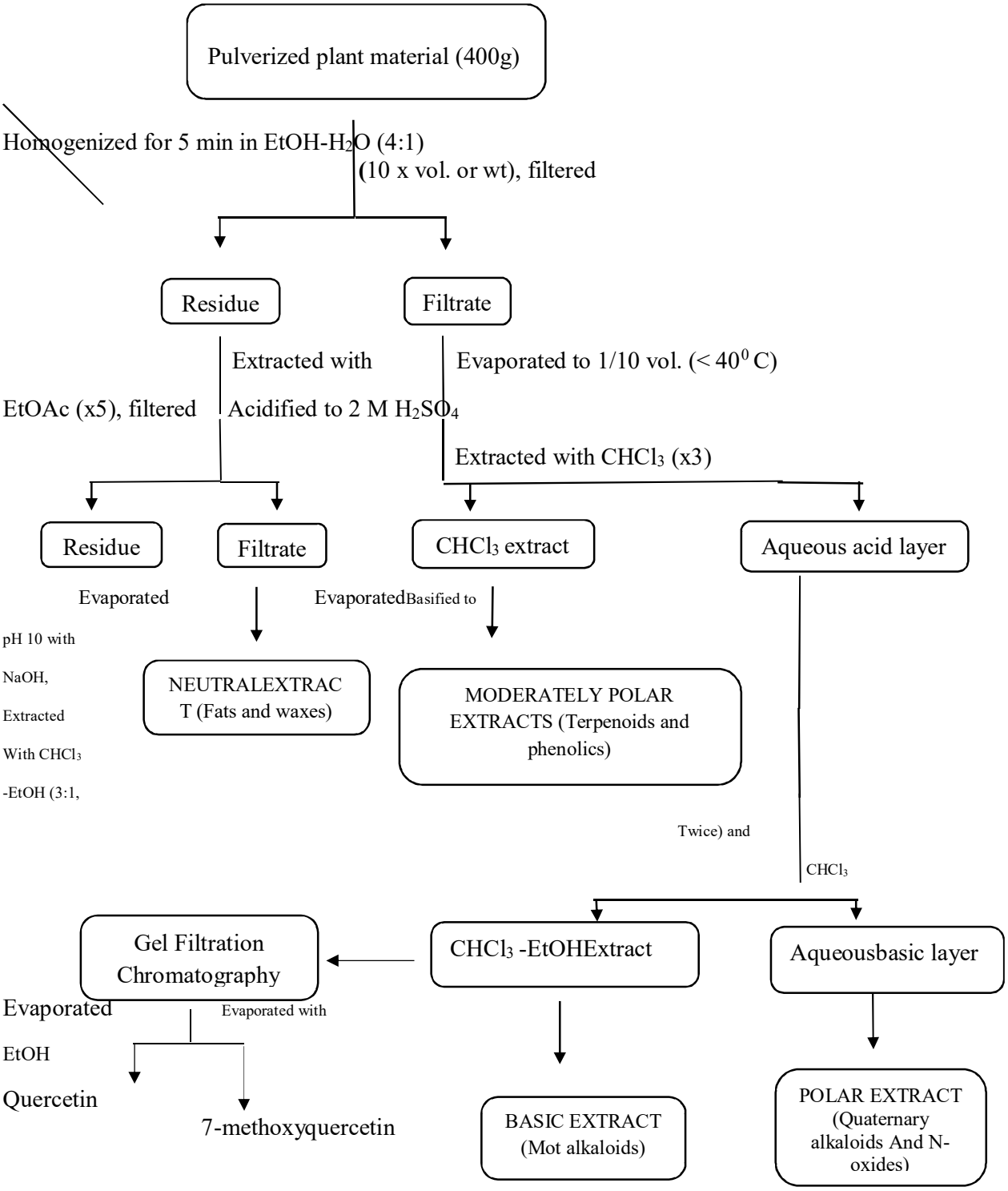

Figure 1: General Procedure for extracting plant tissues and fractionating into different classes according to polarity (Harborne, 1983)

Four extracts were obtained; the ethyl acetate (EA= 7.0g), Chloroform (CHL= 7.5g), Chloroform- ethanol (CE=1.14g) and ethanol (EE=15.6g).

Combination Effect

Combination effect of the compounds with Ciprofloxacin was determined according to the National Committee for Clinical Laboratory Standard (NCLSI, 2011). A volume of 50µl of Quercetin and 7-methoxyquercetin from a stock solution (0.1 mg/ml) was combined with 50µl of Ciprofloxacin that has already been prepared from stock solution (30 µg/ml) and added to each well. The plates were incubated at 37^0C for 18-24 hrs. Synergistic effect was considered when combinations of the extracts with ciprofloxacin exhibited enlargement of combined inhibition zone diameter size by 0.5mm (Ahmad and Aqil, 2007).

Results

Combination Effect

The result of combination therapy of the compounds with ciprofloxacin is as shown in Table 1 and 2

Table 1: Zones of inhibition of the synergistic effect of Quercetinwith Ciprofloxacin

Organism	Concentration of compound (mg/ml) + Ciprofloxacin (µg/ml)	
	QUERCETIN (0.05) + CP (15)	**CP (30)**
B. subtilis	35	30
E. coli	37	32
K.	36	30
pneumoniae	35	32
MRSA	35	30
VRSA	35	30
S. typhi		

CP= Ciprofloxacin**,** MRSA= Methicillin resistant Staphylococcus aureus and VRSA= Vancomycin resistant *Staphylococcus aureus*.

Table 2: Zones of inhibition of the synergistic effect of 7-methoxyquercetin with Ciprofloxacin

Organism	Concentration of compound (mg/ml) + Ciprofloxacin (µg/ml)	
	7-METHOXYQUERCETIN (0.05) + CP (15)	CP (30)
B. subtilis	32	30
E. coli	35	32
K. pneumoniae	32	30
MRSA	34	32
VRSA	35	
S. typhi	35	30

Discussions

The compounds showed potent synergistic activity with ciprofloxacin against the tested organisms. The combinations of the compounds with Ciprofloxacin exhibited enlargement of combined inhibition zone diameter size by not <0.5mm.Quercetin and 7-methoxyquercetinpotentiates the antimicrobial activity of 15 µg/ml ciprofloxacin (zone of inhibition ranging from 32-37 mm) as against ciprofloxacin (30 µg/ml) alone (zone of inhibition ranging from 30-32 mm). A number of methoxylated flavones (Stermitz*et al.,* 2002) and isoflavones (Morel et al., 2003) that potentiate the activities of berberine and the synthetic fluoroquinolone antibiotic norfloxacin have been described.In fact, the compounds showed strong synergistic effect with ciprofloxacin even when they do not have any activity against the tested organisms on their own. Plant antimicrobials have been found to be synergistic enhancers in that though they may not have any antimicrobial properties alone, but when they are taken concurrently with standard drugs they enhance the effect of that drug (Kamouto*et al*., 2006).

Conclusion

From the above findings, it can be concluded that quercetin and 7-methoxyquercetin isolated from *Globimetulaoreophila*can be used to enhance the antibacterial activity of ciprofloxacin.

References

Ahmad, I. and Aqil, F. (2007). In vitro efficacy of bioactive extracts of 15 Medicinal plants against ESL-producing multidrug- resistance enteric bacteria. *Microbiological Research.* 162: 264-275.

Chanda, S., Dudhatra, S., Kaneria, M (2010). Antioxidative and antibacterial effects of seeds andfruit rind of nutraceutical plants belonging to the family Fabaceae

family. *Food and Function*. 1:308-315.

Chen J., Zhu, Z., Hu, T. and Zhu, D. (2002) Structure activity of natural flavonoids in radical-scavenging effects. *ActaPharmacologicaSinica*. 23 (7): 667-672.

Darwish, R.M and Aburjai, T.A (2010). Effect of ethnomedicinal plants used in folklore medicinein Jordan as antibiotic resistant inhibitors on *Escherichia coli. BMC Complementary and Alternative Medicine*. 10:9-16.

Fisgin, N.T., Cayci, Y.T., Coban, A. Y., Ozatli, D., Tanyel, E., Durupinar, B. and Tulek, N. (2009). Antimicrobial activity of plant extract Ankaferd Blood Stopper®. *Fitoterapia.* 80:48–50.

Gur, S., Turgut-Balik, D. and Gur, N (2006). Antimicrobial activities and some fatty acids of turmeric, ginger root and linseed used in the treatment of infectious diseases. *World Journal of Agricultural Sciences*. 2:439-442.

Habbal, O., Hasson, S.S., El-Hag, A.H., Al-Mahrooqi, Z., Al-Hashmi, N., Al-Bimani, Z., Al-Balushi, M.S. and Al-Jabri, A.A (2011). Antibacterial activity of *Lawsoniainermis*linn (Henna) against *Pseudomonas aeruginosa. Asian Pacific Journal of Tropical Biomedicine.*1:173-176.

Iwu, M.M., Duncan, A.R. and Okunji, C.O. (1999). Antimicrobials of plants origin. In: Janick, J. (ed.) Perspective on crops and uses. Ashs Press, Alexandria, V.A: 457- 462 *Journal of Natural Product. 55*, 245-248.

Jeong, M., Kim, H. and Cha, J. (2009). Antimicrobial activity of methanol extract from *Ficuscarica*leaves against oral bacteria. *Journal of Bacteriology and Virology*. 39:97-102.

Kamatou, GPP, Van Zyl, R.L., Van Vuuren, S.F., Viljoen, A.M., Figueiredo, A. C., Barroso, J.G., Pedro, L.G. and Tilney, P.M. (2006). Chemical composition, leaf trichome types and biological activities of the essential oils of four related *Salvia* Species indigenous to Southern Africa. *Journal of Essential Oil Research*. 18: 72-79.

Lee, D. Y., Lyu, H. N., Kwak, H. Y., Jung, L., Lee, Y. H., Kim, D. K., Chung, I. S., Kim, S. H. and Baek, N. I. (2007). Isolation of Flavonoids from the fruits of *Cornuskousa Burg. Journal of Applied Biological Chemistry;* 50: 144-147.

Lucy H. and DaSilva E, (1999) Medicinal plants: A re-emerging health aid. *Electronic Journal of Biotechnology.* 2: 56-70.

Morel, C. Stermitz, F. R., Tegos, G. and Lewis, K. (2003). Isoflavones as potentiators of antibacterial activity. *J. Agric. Food. Chem.*51: 5677-5679.

National Clinical and Laboratory Standard Institute (NCLSI) (2011). M100-S21, performancestandards for

susceptibility testing. Twenty-First international supplements Wayne, PA.

Naxhije H., Ariola, D., Klementina, P., Sotir, M., Theni, B. and Erleta, P.(2011). The dynamicsof antimicrobial resistance of *Salmonella typhimurium* isolates. *J IMAB*; 17:111-115.

Negi, B.S. and Dave, B.P. (2010). Evaluation of *in vitro* antimicrobial activity from the leaves extract of *Cassia firstula*Linn. *Journal of Pure and Applied Microbiology*. 4:557-564.

Parekh, J. and Chanda, S. (2007). Antibacterial and phytochemical studies on twelve species of Indian medicinal plants. *African Journal of Biomedical Research*. 10:175-181.

Prescott, H. and Klein, J.O. (2002). *Microbiology* 6th ed. Macgraw Hill Publishers, USA; 808-823.

Sada, H., Sallau, M. S., Musa, A. M. and Habila, J. D. (2016). Isolation, Characterization and Antibacterial Activity of two Flavonoids from the Chloroform-ethanol extract of *Globimetulaoreophila*(Loranthacea e). *Journal of Pharmaceutical Sciences and Pharmacy practice (*in press).

Sharma, L and Kumar, A. (2006). Antimicrobial activity of *Ageratum conyzoides*Linn. A plantwith extra-medicinal value. *Asian Journal of Experimental Sciences*. 20:41-46.

Stermitz, F. R., Seriven, L. N., Tegos, G. and Lewis, K. (2002). Two flavonols from *Artemisa annua* which potentiate the activity of berberine and norfloxacin against a resistant strain of *Staphylococcus aureus. PlantaMedica*. 68: 1140-1141.

Usha, PTA, Jose, S. and Nisha, A.R (2010). Antimicrobial drug resistance - a global concern. *Veterinary World.* 3:138-139.

Vaghasiya, Y., Nair, R. and Chanda, S. (2008). Antibacterial and preliminary phytochemical and physico-chemical analysis of *Eucalyptus citriodora*Hk leaf. *Natural Product Research.* 22:754-762.

Williams C.A. and Grayer R.J. (2004). Anthocyanins and other flavonoids. *Natural Product Reports*. 21:539-573.

Xu, H. X. and Lee, S. F. (2001). Activity of plant flavonoids against antibiotic-resistant bacteria. *Phytotherapy Research*. 15: 39-43.

Yoon, J. I., Bajpai, V. K., Kang, S. C (2011). Synergistic effect of nisin and cone essential oil of *Metasequoiaglyptostroboides* Miki ex Hu against *Listeria monocytogenes*in milk samples. *Food and Chemical Toxicology.* 49:109-114.