PHOTO ACTIVATED BACTERIAL DNA-BINDING ACTIVE RUTACEOUS ALKALOIDS FROM *GLYCOSMIS PENTAPHYLLA* (RETZ.) DC. AND *RUTA ANGUSTIFOLIA* (L.) PERS.

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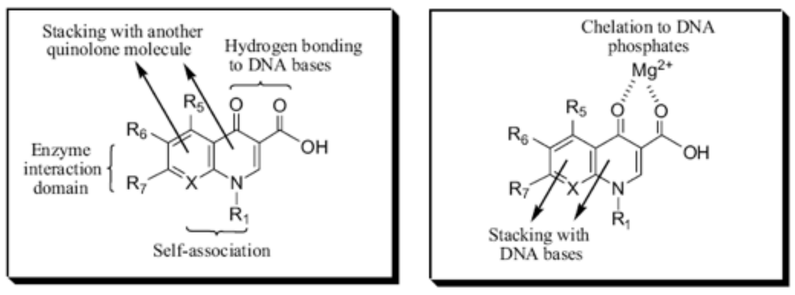
ABSTRACT

Arborine, a quinazoline and graveoline, a 4-quinolone are the antimicrobial active Rutaceous alkaloids isolated from *Glycosmis pentaphylla* and *Ruta angustifolia*, respectively. Both alkaloids possess chromophore with a few structural similarities with the pharmacophore of 4-quinolone antimicrobial agent. Their bacterial DNA-binding activity was assessed by photo activated DNA binding assay and agarose gel electrophoresis. Ten different restriction enzymes which recognise and cleave DNA in a sequence-specific manner were competed by the alkaloids. The DNA binding activity was detected as inhibition of the enzymatic restriction resulting in the detection of uncleaved DNA fragments of the original size. Arborine showed inhibitory activity against the restriction enzymes *Eco*R I, *Pae* I and *Dra* I with the highest intensity of inhibition for *Dra* I which have 5'-TpA sequence. Graveoline was active against *Eco*R I, *Dra* I and *Pst* I. Ciprofloxacin, the second generation of quinolone antimicrobial agent only the inhibitor of *Kpn* I and *Pst* I. The photo activated bacterial DNA-binding activity was in the sequence of arborine>graveoline>ciprofloxacin. This finding revealed the potential of arborine and graveoline as lead compounds for future development of quinolone antimicrobial agents in resolving the antibiotic resistance cases which are globally common nowadays in clinical setting.

INTRODUCTION

The Rutaceous alkaloids particularly the quinolines and quinozolines are the types of quinoline alkaloids that possess the chromophore structures which are similar to the pharmacophore of the conventional 4-quinolone antimicrobial agents. Therefore it is presumed that these types of natural quinoline alkaloids could also share the same activity as the conventional quinolone antimicrobial agents. Although these conventional agents demonstrate an excellent treatment against so many infectious diseases, the emergence of quinolone resistance against some microbes has been a disturbing feature of microbial infection.



Two binding models of quinolone (Emami et al., 2005)

OBJECTIVES

To search for natural quinolone antimicrobial agents by screening the alkaloids for their photo activated DNA-binding activity

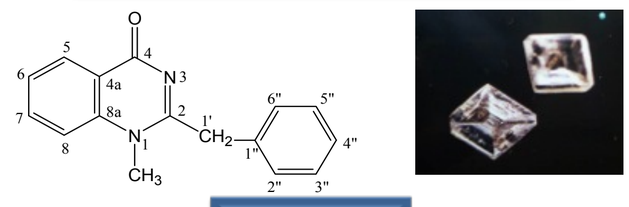
MATERIALS AND METHODS

The plant species

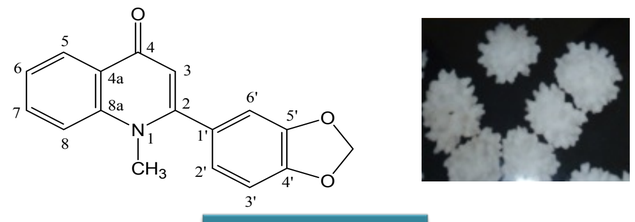
Glycosmis pentaphylla (Retz.) DC.

Ruta angustifolia (L.) Pers.

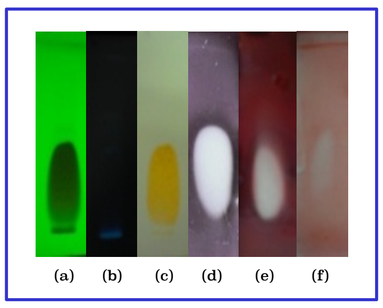
The active alkaloids



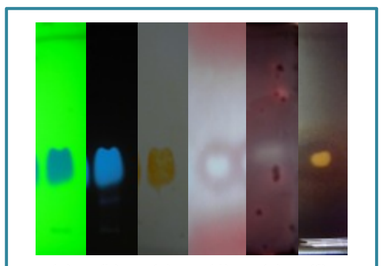
Arborine



Graveoline



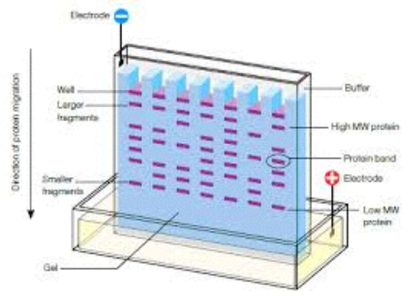
(a) UV_{254}	(b) UV_{366}	(c) Dragendorffs'
(d) *S. aureus*	(e) *E. coli*	(f) *C. albicans*



The antimicrobial profile

In Vitro Photoactivated Bacterial DNA Binding Assay [Hanawa et al., 2004)

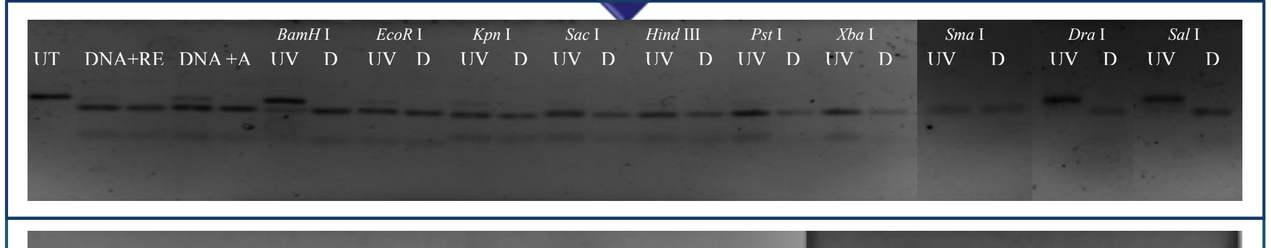
Gel Elecrophoresis



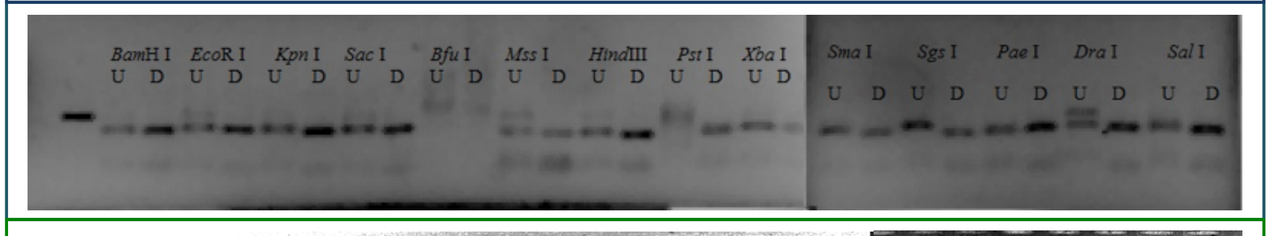
RESULTS

THE BACTERIAL DNA-BINDING

Arborine



Graveoline



Ciprofloxacin

The respective order of photoactivated bacterial DNA-binding activity: arborine>graveoline>ciprofloxacin.

DISCUSSION

- The DNA binding activities were detected as inhibition of enzymatic restriction resulting in the detection of uncleaved DNA fragments of the original size (Hanawa et al., 2004)
- Arborine showed inhibitory activity against the restriction enzymes *Eco*R I, *Pae* I and *Dra* I with the highest intensity of inhibition for *Dra* I which have 5'-TpA sequence.
- Graveoline was active against *Eco*R I, *Dra* I and *Pst* I.
- Ciprofloxacin, the second generation of quinolone antimicrobial agent only the inhibitor of *Kpn* I and *Pst* I.

CONCLUSION

This finding revealed the potential of arborine and graveoline as lead compounds for future development of quinolone antimicrobial agents.

REFERENCES

- Hanawa, F., Fokialakis, N. & Skaltsuonis, A. L., (2004). Photoactivated DNA binding and antimicrobial activities of furoquinoline and pyranoquinoline alkaloids from Rutaceae. *Planta Medica*, *70*, 531-535.
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ACKNOWLEDGEMENT

The authors acknowledge their special gratitude to the Kulliyyah of Pharmacy, IIUM and Ministry of Higher Education Malaysia (MOHE) for financial assistance (FRGS 0207-60) and those whom involved in making this work a success.