SYNTHESIS OF ESSENTIAL OIL DERIVATIVES FOR DEVELOPMENT OF INSECTICIDAL PRODUCTS AGAINST MOSQUITOES AND HOUSEFLIES

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SYNTHESIS OF ESSENTIAL OIL DERIVATIVES FOR DEVALOPMENT OF INSECTICIDAL PRODUCTS AGAINST MOSQUITOES AND HOUSEFLIES

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Public health pest control is a major priority to minimize the infections and transmission of vector-borne diseases in the tropical region. Increased public concern regarding the potential adverse effects of chemical insecticides has prompted the search for alternative methods of pest control. Plant essential oils having a rich source of bioactive chemicals have been considered potent alternatives to conventional insecticides as a natural means of pest control.

The objectives of the present study are to synthesise derivatives of essential oil compounds, menthol, thymol, α-terpineol, geraniol, eugenol, citronellol, cinnamyl alcohol and cinnamic acid and to evaluate their activity against mosquitoes and houseflies. The second is to establish the Structure Activity Relationship (SAR) of compounds with the aim of identifying structural features that are necessary for activity and the third to develop insecticidal products.

Insecticidal properties of oils of *Cinnamomum zeylanicum*, *Cymbopogon nardus*, *Cymbopogon citratus*, *Ocimum gratissimum*, *Ocimum canum*, *Toona ciliata* and *Mentha piperita* have been recognized and the principle active compounds were identified. Acyl, halo acyl, ether, cyclic acetal, epoxide and hybrid derivatives with structures based on insecticidal menthol, thymol, α-terpineol, geraniol, citronellol, eugenol, cinnamyl alcohol and cinnamic acid have been synthesized by using standard reaction conditions. Synthetic derivatives were purified by Dry Column Flash Chromatography and structures were elucidated by ^{1}H and ^{13}C NMR spectral data. Bio-assay followed the WHO standard protocol for *Culex quinquefasciatus*, *Anopheles*

tessellatus and *Aedes aegypti* and topical application method for *Musca domestica.* Anti-mosquito creams/lotions, mosquito coils, repellent candles and housefly baits and liquid sprays were prepared incorporating active compounds and oils and the bio-efficacy was tested in the laboratory and field.

Synthetic derivatives showed enhanced insecticidal activity with relative to the parent compounds. SAR of the compounds identified that lipophilicity of the molecule as one of the key activity enhancing factors. This was highlighted by the increased activity in the ester derivatives of menthol, geraniol, cinnamyl alcohol and cinnamic acid with relative to their analogues containing hydroxyl, ether and carbonyl functionalities. The majority of compounds with aliphatic ester groups, which are less bulky, showed increased activity than its chlorinated and fluorinated compounds. The presence of a nitrogen atom in the esterifying group has retained the insecticidal activity and the replacement of hydroxyl functionality for example with glycerin acetal moiety has increased the activity significantly. Aromaticity is another key factor, which contribute to enhance the activity as seen in thymol. Degree of unsaturation is also contributed to either retain or enhance the activity of α-terpineol and geraniol derivatives. The structurally related analogues have either comparable or higher activity indicating that structural variations contribute positively towards the insecticidal activity. SAR data also indicated that cinnamic acid ester derivatives are less toxic than their parent alcohol moieties.

Field study data of anti-mosquito creams revealed that five formulations showed 100% protection and ten formulations greater than 90% protection in the field with relative to the commercial formulations. It was also found that both citronella and neem oil function as a synergists in above formulations. Bio-assay data of housefly baits indicated that seven baits showed good KT_{50} values with comparison to the reference bait.