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The antimicrobial and toxicity properties of essential oil compounds combined with carrier oils

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Essential oils contain a number of biologically active compounds that have been identified as alternative antimicrobials, however, their use is often limited due to their toxic nature. Carrier oils can reduce the toxicity of essential oils, which raises the question as to whether such activity would extend to the essential oil compounds if used in combination. Thus, this study aimed to investigate the toxicity, and the antimicrobial activity of 21 essential oil compounds in combination with six carrier oils against the ESKAPE pathogen group.

The antimicrobial properties of the essential oil compounds, alone and in combination with carrier oils, were determined using the broth microdilution assay to determine the minimum inhibitory concentration (MIC) against *Enterococcus faecium* (ATCC 27270), *Staphylococcus aureus* (ATCC 25923), *Klebsiella pneumoniae* (ATCC 13883), *Acinetobacter baumannii* (ATCC 17606), *Pseudomonas aeruginosa* (ATCC 27853) and *Escherichia coli* (ATCC 8739) reference strains. A yeast reference strain, *Candida albicans* (ATCC 10231), was also included. The toxicity was determined using the brine shrimp lethality assay. The interactive profiles of the combinations of the compounds and carrier oils was determined by calculating the fractional inhibitory concentration index (ΣFIC) (MIC studies) and the fractional percentage mortality index (ΣFPM) (toxicity studies). The selectivity index (SI) of the combinations showing synergy in the broth microdilution assay was investigated. The time-kill effects of the essential oil compound: carrier oil combination that was synergistic in the broth microdilution assay and that demonstrated reduced toxicity, was further evaluated.

Of the combinations tested in the broth microdilution assay, 3% resulted in synergy (ΣFIC ≤ 0.50), with the compound thymoquinone and the carrier oil *Prunus armeniaca* demonstrating broad-spectrum synergistic activity. The carrier oils reduced the toxicity of the compounds, where at 24 and 48 hrs, the combinations showed 8% and 6% synergy, respectively. *Calendula*

officinalis and *P. armeniaca* carrier oils were responsible for most of the reduced toxicity observed. The compound thymoquinone was present most often in combinations which showed SI values > 4. The combination of *Aloe vera* with α-terpinene demonstrated synergy in the broth microdilution assay (ΣFIC value of 0.41), as well as reduced toxicity (ΣFIC value of 0.49) and was thus evaluated in the time-kill assay. The combination provided bacteriostatic activity over 6 hrs.

This study provides evidence of the essential oil compound: carrier oil interactions where favourable several combinations such as *A. vera* with α-terpinene, *P. armeniaca* with thymoquinone, *P. americana* with thymoquinone and *H. perforatum* with *p*-cymene, could be identified as ideal candidates for further research into developing novel combination therapy against the ESKAPE pathogens. Furthermore, the interactions demonstrate the added value of carrier oils in combination with several essential oil compounds.