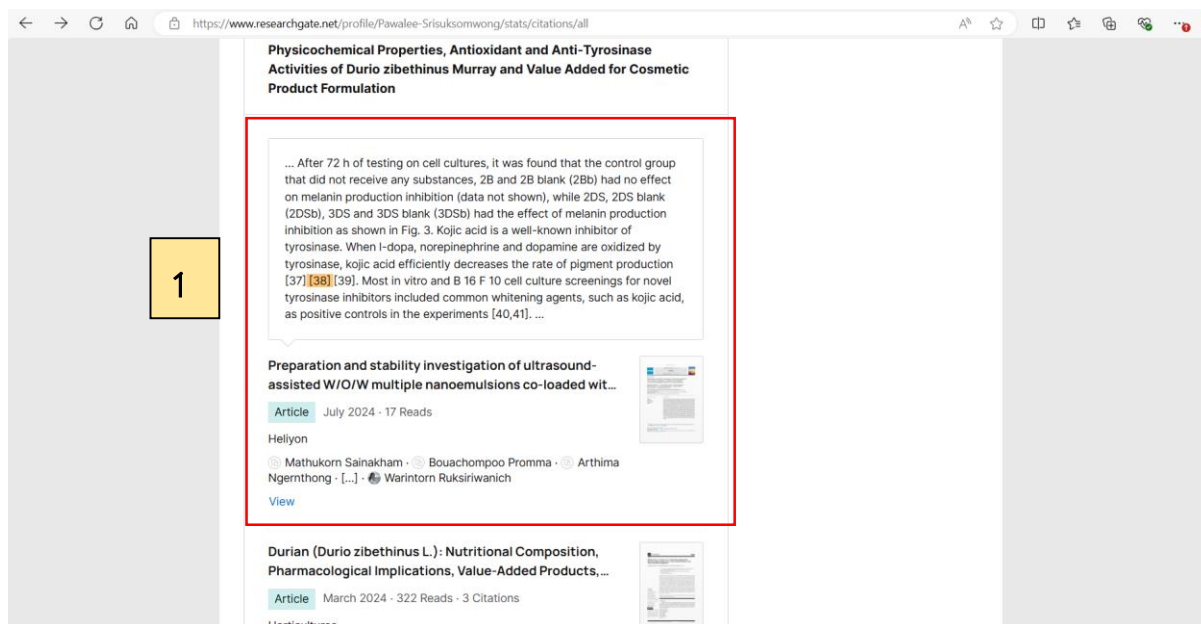


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Research article

Preparation and stability investigation of ultrasound-assisted W/O/W multiple nanoemulsions co-loaded with hydrophobic curcumin and hydrophilic arbutin for tyrosinase inhibition

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ABSTRACT

In the present, whitening products are most popular in the cosmetics market, and nanoemulsions are effective drug delivery systems through the skin. The objective of this study was to investigate multiple nanoemulsion formulations for lightening skin effects. The method of this study was the selection of active compounds based on synergistic tyrosinase inhibition activity, formulation preparation by low and high energy methods, physicochemical property determination, stability test, cell toxicity, and anti-melanogenesis in cell culture. From the results, it was found that tyrosinase inhibition with substrate L-tyrosine from the mixture of curcumin and alpha-arbutin gave the highest activity with an IC_{50} of $63.58 \pm 4.99 \mu M$, showed a synergistic effect at a CI value of 0.99, and selected these compounds to develop formulations by the low energy method. However, the most formulations prepared by this method were unstable and phase separated, while the high energy method gave the most formulations with good properties, which were selected for further investigation. The best formulation was 2DS which showed internal droplet morphology in the range of nanometers under a TEM microscope. For 3 months stability test, the formulations had no phase separation and gave the slightly changed values of particle size, polydispersity index (PDI), zeta potentials, and pH values. In addition, multiple nanoemulsions also enhanced the stability of active compounds, with the highest percentage of remaining con-

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