The present study revealed the optimization of nanoemulsion containing palm oil derivatives and Parthenium hysterophorus L. crude extract (PHCE) as pre-emergence herbicide formulation against Diodia ocimifolia. The nanoemulsion formulation was prepared by high energy emulsification method, and it was optimized by mixture experimental design (MED). From the optimization process, analysis of variance (ANOVA) showed a fit quadratic polynomial model with an optimal formulation composition containing 30.91% of palm kernel oil ester (PKOE), 28.48% of mixed surfactants (Tensiofix and Tween 80, 8:2), 28.32% of water and 12.29% of PHCE. The reading of both experimental and predicted particle size in the verification experiment were acceptable with a residual standard error (RSE) was less than 2%. Under the optimal condition, the smallest particle size obtained was 140.10 nm, and the particle was shown by morphology analysis to be spherical and demonstrated good stability (no phase separation) under centrifugation and different storage conditions (25 ± 5°C and 45°C). Nanoemulsion stored for 60 days exhibits monodisperse emulsion with a slight increase of particle size. The increase in particle size over time might have contributed by Ostwald ripening phenomenon which is shown by a linear graph from Ostwald ripening rate analysis. In the in vitro germination test, P. hysterophorus nanoemulsion (PHNE) was shown to cause total inhibition of D. ocimifolia seed at lower concentration (5 g L-1) as compared to PHCE (10 g L-1). The finding of the research could potentially serve as a platform for the development of palm oil based formulation containing plant crude extract for green weed management.

**Keyword:** P. hysterophorus; Herbicide; Nanoemulsion; Natural; Optimization; Palm oil esters; Weed management