

# Zerumbone Derivatives: New Candidates for Cancer Treatment

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Being a sesquiterpene isolated from essential oil of *Zingiber zerumbet* Smith (bitter ginger), a widespread plant in Vietnam, zerumbone (1) is currently considered as a potential candidate for new anticancer medicines thanks to its strong anticancer activity. Nonetheless, due to its poor polarity, zerumbone has not been used in medication yet. Our project aimed to synthesize new derivatives with better anticancer activity and bioavailability but low toxicity by combining zerumbone with different amines, which are partial structures of several anticancer compounds. We have isolated zerumbone from the essential oil of the rhizomes of *Z. zerumbet* with much better yield than previously reported. Then, the intermediate compound (2) was successfully prepared by the reaction between zerumbone and N-Bromosuccinimide. Finally, nine new derivatives (3a-3i) were synthesized by nucleophilic substitution reaction between (2) and eight different amines. Structures of all compounds were determined by HR-MS, 1D and 2D NMR spectroscopy. These derivatives have been synthesized with good yield and much stronger anticancer activity than that of zerumbone on six cancer cell lines (Hep-G2, LU, Jurkat, Hela, SW 480 and MCF-7). Especially, the activity of 3a is ten times as strong as that of zerumbone. 3b also shows impressive anticancer activity against Hep-G2 cells with IC<sub>50</sub> value of 0.58 µg/mL. 3a and 3i have been examined for antitumor activity on soft agar. The result showed that both of them are capable of decreasing the intensity and the size of tumors. This finding of new zerumbone derivatives suggests them as new candidates for anticancer treatment. Keywords: *Zingiber zerumbet* Smith, zerumbone, anticancer, derivatives, amines

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