ABSTRACT: Three new acetophenone dimers or Acronychia-type acetophenones, acropyrone (1), acropyranol A (2), and acropyranol B (3), were isolated from the trunk bark of Acronychia pedunculata and structurally characterized, together with four known acetophenone dimers, acrovestone (4), acrovestenol (5), acrofolione A (6), and acrofolione B (7), the acetophenone monomer acronyline (8), and four furoquinoline alkaloids. The chemical structures of the new isolated compounds were elucidated unambiguously by spectroscopic data analysis. The cytotoxic activities of the isolated acetophenone dimers were evaluated against the DU145 prostate and A2058 melanoma human cancer cell lines as well as the NHDF normal cell line. Acrovestone (4) and acrovestenol (5) exhibited substantial cytotoxicity, with IC50 values of 0.38 and 2.8 μM against A2058 melanoma cells as well as 0.93 and 2.7 μM against DU145 prostate cancer cells, respectively.

Acronychia is a genus of the plant family Rutaceae consisting of 42 species. The roots, stems, leaves, and fruits of certain species in this genus have been used for centuries in eastern traditional medicine for the treatment of asthma, cough, diarrhea, itchy skin, pain, rheumatism, scales, sores, and ulcers and also for their antihemorrhagic, antipyretic, and aphrodisiac activities. In particular, Acronychia pedunculata (L.) Miq. (= Acronychia laurifolia Bl.) is an evergreen tree distributed widely in rainforests of India, Sri Lanka, Indonesia, Malaysia, and southern mainland China. According to previous studies, the most common secondary metabolites isolated from A. pedunculata are furoquinoline alkaloids and prenylated acetophenone derivatives, of which the latter are mainly prenylated acetophenone monomers. Special attention may be given to the prenylated acetophenone dimers since only a few have been reported and because these occur exclusively in the genus Acronychia, indicating their value as chemotaxonomic markers of the genus.

Biological evaluation of extracts of A. pedunculata has shown significant antimalarial, antibacterial, and antifungal activities as well as cytotoxic effects for several cancer cell lines. Biological interest in prenylated acetophenones has focused on their antioxidant, cytotoxic, and anti-inflammatory activities, while the acetophenone dimers have been assessed for cytotoxicity against numerous cancer cell lines, with acrovestone reported to exhibit significant cytotoxicity. Despite their potential chemotaxonomic and biological importance, only a small number of acetophenone dimers have been isolated and biologically evaluated from the genus Acronychia.

In the present study, a phytochemical investigation is reported of an Et2O extract from the trunk bark of A. pedunculata focused on the isolation of acetophenone dimers and the biological evaluation of these compounds. Specifically, three new Acronychia-type acetophenones were isolated and structurally identified, namely, acropyrone (1), acropyranol A (2), and acropyranol B (3). Moreover, four known acetophenone dimers, acrovestone (4), acrovestenol (5), acrofolione A (6), and acrofolione B (7), and the acetophenone monomer acronyline (8) were obtained. All Acronychia-type acetophenones were tested for their cytotoxic...