SUMMARY

Synthesis and biological activity of 2,3,5,6,7,8,9-substituted 2,3,4,9-tetrahydrofuro[2,3-*b*]quinolin-4-ones

Chien-Ping Chang

Graduate Institute of Pharmaceutical Chemistry
China Medical College

A series of 2,3,5,6,7,8,9-substituted 2,3,4,9-tetrahydrofuro[2,3-*b*]quinolin-4-ones has been synthesized and assigned by their spectra data. All of these synthetic compounds were evaluated for antiarrhythmic, anti-platelet, anti-allergic and anti-inflammatory activity by inhibition tests of mast cell degranulation, neutrophil degranulation, and neutrophil superoxide formation. Among these tested results, *N*-*o*-fluorobenzyl-6-ethyl-2,3,4,9-tetrahydrofuro-[2,3-*b*]quinolin-3,4-dione (**133**) exhibited significantly inhibitory activity on fMLP-induced neutrophil degranulation (IC_{50}= 20.5± 2.2 μM). *N*-*p*-Methoxy-benzyl-6-chloro-2,3,4,9-tetrahydrofuro[2,3-*b*]quinolin-3,4-dione (**144**) inhibited on fMLP-induced neutrophil superoxide formation (IC_{50}= 15.4± 1.3 μM). *N*-*p*-Chlorobenzyl-7-ethyl-2,3,4,9-tetrahydrofuro[2,3-*b*]quinolin-3,4-dione (**76**) (IC_{50} = 26.8± 0.8 μM), *N*-*m*-methoxybenzyl-7-chloro-2,3,4,9-tetrahydrofuro[2,3-*b*]-quinolin-3,4-dione (**87**) (IC_{50} = 28.3± 1.3 μM) and *N*-*p*-chlorobenzyl-7-chloro-2,3,4,9-tetrahydrofuro-[2,3-*b*]quinolin-3,4-dione (**94**) (IC_{50} = 28.3± 3.7 μM) exhibited significantly inhibitory activity on LPS-induced RAW 264.7 cell accumulation of nitrite in medium. *N*-*o*-Methylbenzyl-7-ethyl-2,3,4,9-tetrahydrofuro[2,3-*b*]quinolin-3,4-dione (**69**) exhibited significantly inhibitory activity to LPS-induced N9 cell accumulation of nitrite in medium (IC_{50} = 11.9± 0.7 μM).

However, there is no significantly inhibitory activity on compound 48/80-induced mast cell degranulation, PMA-induced neutrophil superoxide formation, TNF-α and PGE_2 formation in medium.

Among compound **68-79,** *p*-chlorobenzyl-7-ethyl-2,3,4,9-tetrahydrofuro-[2,3-*b*]quinolin-3,4-dione (**76**) showed the most significant activities on antipletelet tests in higher concentraction (100 μg/ml).

N-Benzyl-7-ethoxy-2,3,4,9-tetrahydrofuro[2,3-*b*]quinolin-3,4-dione (**248**) exhibited the most significant activities on antiarrhythmic tests.

Meanwhile, some of these synthetic compounds were further evaluated for their antipletelet activity. Those activities are still under investigation and the further results will be reported later.