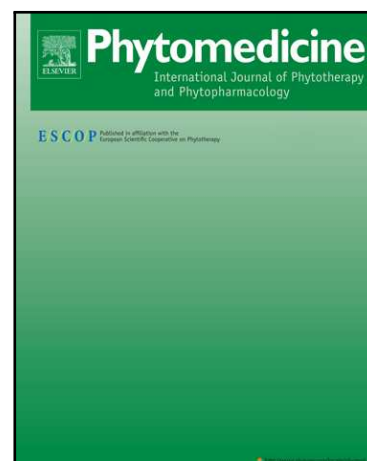


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Flavonoids isolated from Tibetan medicines, binding to GABA_A receptor and the anticonvulsant activity

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Abstract:

Background: Our previous studies on *Asterothamnus centrali-asiaticus* Novopokr. (*ACN*) and *Arenaria kansuensis* Maxim. (*AKM*) had led to the isolation of some phytochemical constituents and evaluation of anticonvulsant effect based on their extracts. *ACN* and *AKM* have been widely used in traditional Tibetan herbs for neuropsychiatric diseases and cardiopulmonary disorders.

Purpose: The purpose is to investigate structure-activity relationships of flavonoids isolated from *ACN* and *AKM*, for binding to the benzodiazepine site (BZ-S) of γ -aminobutyric acid type A (GABA_A) receptor complex, and to search for anticonvulsant compounds without undesirable effects such as myorelaxation and sedation.

Study design and methods: The affinities of these flavonoids for the BZ-S of GABA_A receptors were determined by [³H]flunitrazepam binding to mouse cerebellum membranes *in vitro*. And the anticonvulsant, myorelaxant and sedative effects were determined by pentylenetetrazol (PTZ)-induced seizure and electrogenic seizure protection, rotarod test and locomotor activity test, respectively.

Results: Fifteen and thirteen flavonoids were isolated from *ACN* and *AKM*, respectively. Structure-activity relationships analysis indicated that 6-and/or 8-OMe flavones exhibited the most potent binding affinity to GABA_A receptors. Furthermore,

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