The Pharmacology of Chlormethiazole:  
A Potential Neuroprotective Agent?

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**ABSTRACT**

Chlormethiazole is a thiazole derivative with a long history of use as a sedative agent. The mode of action of the drug has been partly worked out and has been established with recognition that its mechanism of action involves potentiation of GABA activity, the major intrinsic inhibitory neurotransmitter. Animal models of stroke ranging from rodents to primates have suggested an optimistic role for chlormethiazole in preventing both anatomical and functional deleterious effects of stroke. Phase III clinical trials, therefore, proceeded but unfortunately with very little success. Recently, the animal models have been revisited in an attempt to identify causes for this discrepancy between the results from preclinical and clinical studies. This review studies the pharmacological roots of chlormethiazole from its origin through to its licensed and novel applications. Emphasis is placed on discussing the animal experiments which led to its grooming as a neuroprotective agent and also on the human trials. The review seeks to explain the discrepancies between animal and human studies, which include short survival times of experimental subjects, speed of drug administration and fundamental differences between species. The primate model of stroke perhaps offers the nearest alternative to phase III trials and has recently been used to compare a number of newer neuroprotective agents with greater efficacy than chlormethiazole. In addition, novel approaches involving human neurochemical analyses *in vivo* are described which may help bridge the gap between animal models and future phase III trials.

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