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A Pharmacological Appraisal of the Guanidines

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The first pharmacological interest in the guanidines started some 30 years ago after the discovery of the bioactivities of hydroxy urea and guanidine in medicinal fields of cancer and virology. Subsequently, several investigations explored the bioactivities of a wide variety of guanidine-like structures. Several drugs such as the cyanoguanidines, e.g. pinacidil and cimetidine have found clinical application in the treatment of hypertension and peptic ulcer. The last decade experienced research of known and novel guanidine derivatives in various new medicinal applications in view of their interactions with enzyme systems such as xanthine oxidase and nitric oxide synthase. These properties revealed their potential to afford neuroprotection in the advent of brain injury.

Our investigations have been directed towards the pharmacology of guanidine derivatives in the fields of HIV/AIDS, α_2 adrenoreceptors, electron acceptors at the xanthine oxidase enzyme and ischaemic heart disease. These investigations revealed protective properties of guanidines on myocardial ischaemia and reperfusion in rats against induced myocardial necrosis and life-threatening arrthythmias. Subsequent, non-human primate (*Papio ursinus)* studies on cerebral perfusion while also monitoring of the cardiovascular parameters showed no significant cerebral perfusion effects using the split-dose single photon emission computed tomography (SPECT) at the dose and time-schedules selected for these studies. Negative chronotropic effects and changes in blood pressure were induced in the primate in these studies, thus supporting the rodent data.

In conclusion guanidines have shown remarkable therapeutic potential of over three decades and reaching even clinical status. Our current studies extended the potential of the guanidines towards disorders of the brain and heart. The guanidine structure has proved to be an important scaffold in the design and development of clinically important drugs and novel compounds could in the future add to the therapeutic range already in existence.