MEMOGAIN; A NOVEL ANTIDEMENTIVE DRUG PROMISING HIGHER EFFICACY AND LOWER GASTROINTESTINAL SIDE EFFECTS THAN CLASSICAL CHOLINESTERASE INHIBITORS

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The cholinesterase inhibitors (ChE-I) approved for treatment of AD are known to produce high levels of gastrointestinal side effects, need to be uptitrated in the patient over months to efficacious doses, and are still not well tolerated. Moreover, their efficacies are dissatisfactorily low. To overcome these limitations, we have produced by chemical modification a pro-drug of the ChE-I galantamine with dramatically improved brain penetration. We have chosen galantamine because of its dual mode of action as ChE-I as well as allosteric potentiating ligand (APL) of the nicotinic acetylcholine receptor. Having arrived in the brain, the pro-drug is enzymatically cleaved to produce much higher levels of the active drug galantamine than is achieved by oral administration of the same doses of unmodified drug. As demonstrated in various animal studies, intranasal administration of this pro-drug Memogain results in significantly larger cognitive enhancement and practically no gastrointestinal side effects, as compared to the same doses of orally administered galantamine. Higher efficacy is achieved by higher drug levels at target sites in the brain, and the much lower side effects potential by reduced drug levels in the periphery, in combination with avoidance of the gastrointestinal passage. In conclusion, combining a pro-drug approach with intranasal delivery appears to be a suitable means of dramatically improving both, the medical benefit and the patients compliance, of galantamine.