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| **Title:** Prodrugs containing albumin binding probes |
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| **Summary:** |
| Albumin binding probe for extending the lifetime of drugs.  Most polypeptide drugs, in particular non-glycosylated proteins of molecular mass less than 50 kDa, are short-lived species *in vivo* having circulatory half lives of 5-20 min. Drug association with endogenous albumin may be suitable for designing an approach to protract the action *in vivo* of, potentially, any short-lived peptide/protein drug. In doing so two principal obstacles must be overcome: (1) following its conjugation, the probe introduced into a peptide or a protein should have sufficient affinity to albumin to manifest prolonged action *in vivo*, and (2) in case such covalent introduction results in an inactive product, the latter should be capable to undergo slow reactivation at physiological conditions. The present invention relates to engineering prolonged-acting prodrugs employing an albumin-binding probe that undergoes slow hydrolysis at physiological conditions. |
| **Applications:** |
| * Turning short-lived amino-containing drugs into inactive reactivable prodrugs having prolonged lifetime profiles *in vivo* |
| **Advantages:** |
| * The albumin-binding probe enables to prolong the action of any amino containing molecule *in vivo*, without the drawback of inactivation that often occurs upon such derivatization * Conjugate reactivation takes place in body fluids at a slow rate, with a desirable pharmacokinetic pattern |
| **Technology's essence :**  Since albumin is long-lived *in vivo*, drugs and endogenous substances that tightly associate with it have lower clearance rates than that of the unbound substances, and exhibit prolonged lifetime profiles *in vivo*. The present invention is based on a concept according to which a long chain fatty acid (LCFA) like albumin-binding compound is covalently linked to a short-lived amino-containing drug to form a non-covalent drug conjugate capable of associating with albumin *in vivo*, i.e., a long-lived prodrug that gradually releases the pharmacologically active constituent. This approach has been successfully implemented with several drugs (e.g. insulin, exendin and gentamicin). |