Towards drug delivery systems triggered by ion-selective interactions

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Achieving well controlled drug delivery is important for effective, safe and convenient administration of drugs to the site of intended action. Active, ion triggered drug delivery is of high interest however, most of the systems proposed respond to change in H^+ ions concentration. We developed a system that allows release of drug ions selective in response to change in the concentration of trigger ions – others that hydrogen ions.

The approach herein proposed [1] is inspired by ion-selective sensors operation principle. A drug delivery system offered allows release of a charged ion drug from a lipophilic polymer in response to ion-selective interactions of trigger ions from solution with ionophore present in the polymer. Spontaneous and stoichiometric incorporation of trigger ions driven by preferential binding to uncharged ionophore results in charged drug ions release to preserve electroneutrality. This requires preloading of the polymer matrix (apart from ionophore selective to trigger ions) with tailor made ion-exchanger containing drug ions.

The idea was verified on a model example: as drug ions - methylene blue cations (Mb^+) were applied. The Mb^+ containing ion exchanger salt: methylene blue - tetrakis[3,5-bis(trifluoromethyl)phenyl]borate, Mb-TFPB, was prepared. Mb-TFPB was loaded into the polymeric phase together with model potassium ions ligand - valinomycin. Thus, obtained system allows using potassium ions as trigger to release the model drug ions to solution. Both polymeric films and nanofibers were tested to demonstrate the effect of format of the applied lipophilic phase on the rate of release of the drug ions.

The herein proposed approach was also further developed to allow doxycycline delivery in response to change in potassium ions concentration in solution.

References:

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