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Detoxifying emulsion for overdosed aspirin intoxication

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ABSTRACT

Aspirin overdose could lead to intoxication, with the clinical manifestations of vomit, pulmonary edema and severe dyspnea. Stomach washing, emetics and activated charcoal are the common treatments with a limited efficiency for the intoxication. In this study, an active emulsion for aspirin intoxication was prepared with the detoxifying efficiency of 100% in less than 15 min, with the conditions of dodecane used as the oil phase, 8% Abil EM90 as the surfactant and 0.1 mol/L sodium hydroxide as the inner aqueous phase in a volume ratio of 2 between internal aqueous phase and the oil phase.

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1. Introduction

Aspirin, discovered by Arthur Eichengrun, a chemist with the German company Bayer (Sneader, 2000), as a common medicine with the effective component of acetylsalicylic acid in daily life is usually used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti-inflammatory medication. As a common pain-killer medicine, aspirin administered in a single dose beyond the prescription amount probably causes the acute intoxication. Patients in acute aspirin intoxication are usually treated by gastric lavage or activated charcoal in the emergency room. However, these treatments are not very effective and intolerable for the patients. Therefore, it is necessary and challengeable to seek for an efficient treatment without side effects for aspirin intoxication.

Emulsion is usually composed of surfactant, carrier (extractant), oil and inner water phases. With large specific surface areas and high selectivity, emulsion is applied to recover the organics (Pan, 2006) in the wastes or to exert the sustained-release function of drug (Liu, 2006) or to remove the toxins from the organisms (Grosber-Manon, 2008). Frankenfeld et al. (1978) and Chiang et al. (1978) prepared emulsions to detoxify the overdosed drugs. Drugs were rapidly removed by the detoxifying emulsion into the internal water phase in a very short time, and the trapped toxic remained inside of membrane during the metabolism, and finally excreted out of the body.

Thus, emulsion is a prospective treatment for drug intoxication. In this paper, an active emulsion system is proposed with an aim of removing overdosed aspirin rapidly and safely.

2. Principles

The main effective component of aspirin is acetylsalicylic acid. As a weak acid, acetylsalicylic acid ionizes in the aqueous solution.

$$AH \xrightarrow{K_a} A^- + H^+ \quad (1)$$

AH stands for acetylsalicylic acid (ASA).

The ionization constant K_a is:

$$K_a = \frac{[H^+][A^-]}{[AH]} \quad (2)$$

In ASA solution, the total content of ASA is expressed as:

$$c_{AH} = [AH] + [A^-] = \left(1 + \frac{K_a}{[H^+]}\right)[AH] \quad (3)$$

Thus, at equilibrium, the ratio of the non-dissociated form of ASA in the whole content of ASA in the solution is α:

$$\alpha\% = \frac{[AH]}{c_{AH}} \times 100 = \frac{[H^+]}{[H^+] + K_a} \times 100 \quad (4)$$

pH influences the existing form of ASA remarkably.

When pH < 2, more than 90% in the solution is the non-dissociated form of ASA; pH > 6 renders most ASA dissociating into ions (A^-) (Fig. 1).

In the acidic solution (gastric fluid), most ASA thus is the non-dissociated form. When ASA solution contacts with emulsions, in theory, the carrier (TOA chosen in this study) in the membrane phase complexes with ASA (AH) (Eq. (5)) and carries it via the

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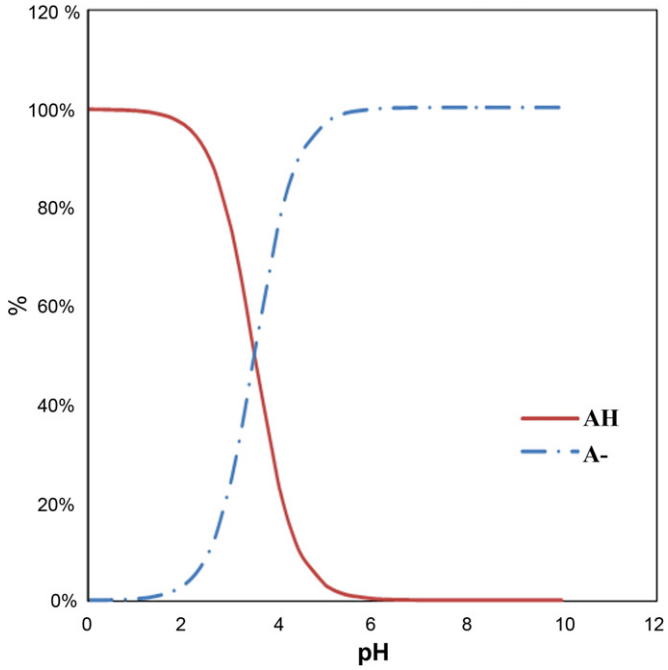


Fig. 1. The effect of pH on the existing forms of ASA in the solution.

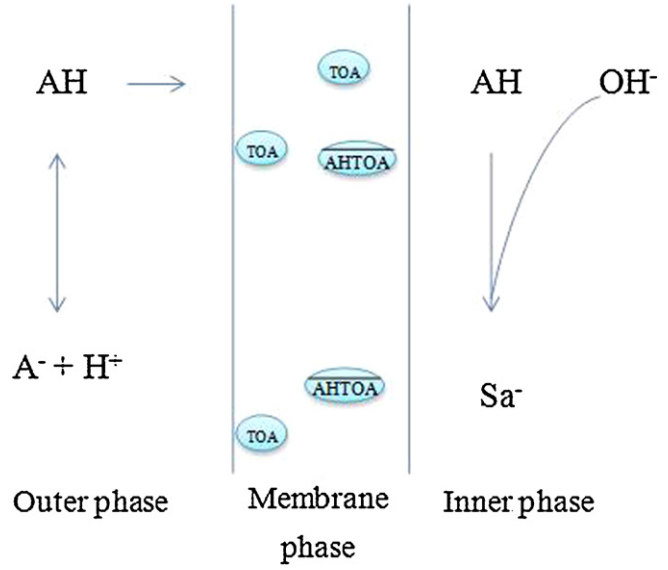
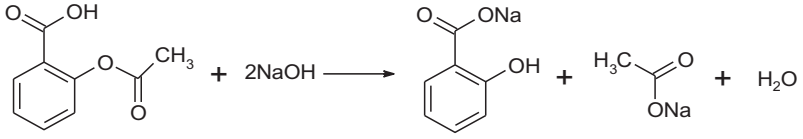


Fig. 2. The sketch of ASA detoxification by the active emulsion.

membrane into the internal side of membrane where the complex of extractant and ASA (AHTOA) decomposes. The carrier is regenerated back to the external interface and ASA is trapped into the internal solution, see Fig. 2.

$$AH + TOA \rightarrow \overline{AHTOA} \quad (5)$$

NaOH solution is the internal aqueous phase of emulsions, because it exhausts acetylsalicylic acid quickly, maintaining a high concentration gradient of ASA through the membrane. The exhausted process is an irreversible reaction like following:



(6)

The salicylate is not soluble in the membrane, so at the internal interface of membrane, acetylsalicylic acid converts into salicylate which is trapped in the inner aqueous phase.

According to the detoxification, in vitro studies were conducted under different conditions, such as carrier and surfactant, and the pH of the external phase of acetylsalicylic acid is supposed to be around 1.5.

3. Materials and methods

3.1. Reagents

Dodecane (ACROS organics) was used as the oil phase. Abil EM90 (Degussa Goldschmidt Gmbh Germany), a cetyl PEG/PPG-10/1-dimethicone with a molecular weight of 13,000, was used as the surfactant; and trioctylamine (TOA from ACROS organics), was used as the carrier. NaOH as the inner aqueous phase was from Panreac QUIMICA SAU and hydrochloric acid (VMW international) diluted into pH 1.5 was the solution to solve aspirin. Acetylsalicylic acid (aspirin) was from Fluka chemical GmbH. All the reagents are analytical pure.

3.2. Preparation of emulsion

The detoxifying emulsions were prepared as following: dodecane containing Abil EM90 and TOA was measured with a certain volume in the beaker; NaOH solution with a certain volume was slowly added into the organic phase under the emulsification machine (yellow line) at the speed of 13,500 rpm and the mixture was emulsified for 10 min to prepare the W/O emulsion.

3.3. Extraction of acetylsalicylic acid

Because most aspirin are absorbed in the stomach, acetylsalicylic acid (1 g/L) was dissolved in the hydrochloric acid with pH 1.5 (pHM 210 standard pH METER). 40 mL of this solution were mixed with 20 mL emulsion in a beaker under magnetic stirring (300 rpm, IKA Yellow Line MSH basic). 6 mL of aqueous solution were sampled at time intervals. Acetylsalicylic acid concentration was determined with the spectrophotometer (VARIAN Cary50 Scan). The extraction ratio (E) of ASA was calculated as following:

$$E(\%) = \left(1 - \frac{[AH]_t}{[AH]_0}\right) \times 100\% \quad (7)$$

$[AH]_t$ is the concentration of acetylsalicylic acid at t moment, and $[AH]_0$ is the initial concentration of ASA solution.

4. Results and discussion

4.1. Extraction performance of active emulsion

ASA solution was sampled at some interval to confirm the concentration of residual acetylsalicylic acid. The efficiency of emulsion removing ASA is illustrated in Fig. 3. In less than 10 min, the maximum detoxification ratio of ASA by emulsion with TOA as carrier was 80%. After 15 min, however, the extraction efficiency of ASA reduced from 80% to 60%. This variation possibly results from the emulsion composition. Thus, the components of emulsion are requisite to be analyzed respectively.

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