Carbon Dioxide Assisted Production of Formulation for Glutathione Administration

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Introduction

Increasing clinical and epidemiological evidence demonstrates that glutatione (GSH) status is significant in acute and chronic diseases. However, reduced GSH is poorly absorbed and/or oxidized in the gastrointestinal tract. Gamma-glutamyltranspeptidase enzyme breaks down glutathione before any significant amount of the compound can translocate into the blood stream. Large amount of the enzyme is found in the gastrointestinal tract [1,2].

Materials and methods

To improve glutathione after oral administration we have incorporated it into nanoparticles or microparticles of ethylcellulose and/or cellulose acetate phthalate. Commercial FMC's Aquacoat® EC (ethylcellulose) and Aquacoat® CPD (cellulose acetate phthalate) pseudo-latex preparations have been used for the microparticles production. Chitosan (medium molecular weight) was added to the Aquacoat® pseudo-latex mixtures in amount of 5 - 10 % of DM to improve mucoadhesivity of the microparticles. Two methods of the microparticles or nanoparticles preparation were tested and compared – conventional spray drying and the carbon dioxide assisted nebulisation. Tablets prepared from the obtained powders were cured at 60°C for 6 hours at high relative humidity.

Results and discussion

The particle shape and size were determined by using optical and scanning electron microscopy method. The *in vitro* GSH release tests were carried out with powders and tablets (see Fig.1) prepared from the powder preparations under simulated physiological digestion conditions using a dissolution rate test in 0.1N HCl medium simulating the stomach conditions and a simulated intestinal fluid, pH 7,4 at 37°C, successively. The release mechanisms involved polymer relaxation, swelling and GSH diffusion. The nanoparticles or microparticles exhibited good mucoadhesion and showed good GSH entrapment efficiency. Kinetics of GSH release can be adjusted in a wide range by changing Aquacoat® ECD, AquacoatR® CPD and chitosan ratios. Thermal curing of the tablets prepared from the powders has significant effect on the GSH release kinetics.

References:

1. Witschi A, Reddy S, Stofer B, Lauterburg BH. The systemic availability of oral glutathione. *Eur J Clin Pharmacol* **43**(6):667-9, 1992.
2. Pizzorno J.E., Katzinger J.J. Glutathione: Physiological and Clinical Relevance. *Journal of Restorative Medicine* **1**(1):24-37, 2012.

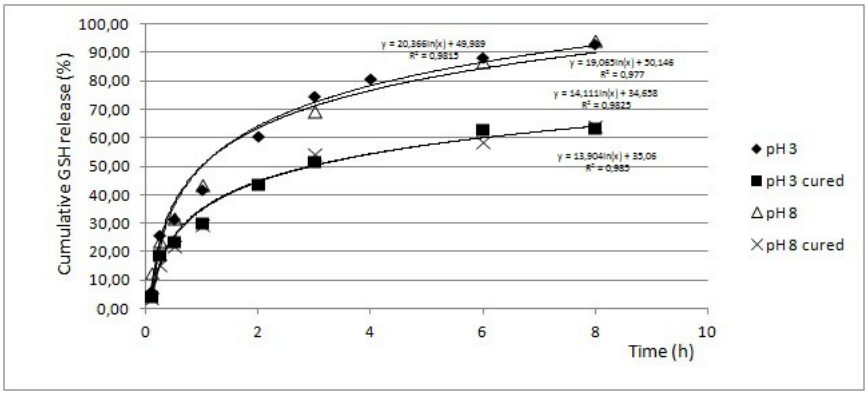

Figure 1: Cumulative GSH release from tablets prepared from the spray-dried powder

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Biosketch

Milos Beran obtained Dipl. Eng. in the Institute of Chem. Technology, Prague - Department of Food Technology in 1985. Since 1985 he has been employed in the Food Research Institute, Prague. He has been a successful leader of many national research projects in the field of food technologies and biotechnologies. At present time he is also engaged in development of technologies for production of nanostructured materials by centrifugal spinning and by supercritical fluid assisted atomization in cooperation with Inovacentrum, Czech Technical University in Prague.

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