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Effects of drying technology and polymers on integrity and biological activity of proteins

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AIMS: Proteins are fragile molecules due to their chemical and physical instabilities. Therefore, stabilisation of the three dimensional structures of proteins is essential for proteins to induce therapeutic effect. Aims for this work are to apply spray drying and freeze drying technologies with excipients namely polyvinyl pyrrolidone and methacrylic acid polymers to maintain integrity, stability and biological activity of lysozyme and trypsin, as model proteins.

METHODS: Proteins without and with excipients in ratios of 1:0.2 and 1:0.5 are dissolved in distilled water and the solutions were spray-dried using Buchi spray drier and freeze-dried via VirTis freeze drier. The commercial (control) and processed proteins were characterized for their: biological activity via enzymatic assay; secondary structure using Fourier-Transform Infrared (FT-IR); morphology via Scanning Electron Microscopy (SEM); Thermal behaviours and folding reversibility using solid Differential Scanning Calorimetry (DSC) and solution DSC, respectively. Also, the prepared formulations were subjected to stability studies at high relative humidity (RH=76%) and high temperature (50°C, for 60min).

RESULTS AND DISCUSSION: Polyvinyl pyrrolidone polymer with both spray dried and freeze dried proteins better maintained bioactivity and integrity of trypsin and lysozyme after drying compared with methacrylic acid polymers. Also, lysozyme-polyvinyl pyrrolidone (1:0.5) and trypsin- polyvinyl pyrrolidone (1:0.2) maintained significant ($p<0.05$) protein activity after storage at high RH and at high temperature compared to all dried protein formulations without and with excipients. These results indicate the protective role of the polyvinyl pyrrolidone on both proteins after drying.

For protein- polyvinyl pyrrolidone formulations, FT-IR exhibited small shift in amide I peaks. SEM revealed different morphologies with different polymers used. Presence of polyvinyl pyrrolidone led to smoothness of surface of spray-dried and freeze-dried lysozyme particles and the size of particles was larger for trypsin particles compared to lysozyme particles. Solid DSC showed decrease in denaturation temperature of lysozyme after processing with excipients in contrast to trypsin samples which showed increase thermal stability in solid state. Spray dried and freeze dried trypsin and lysozyme with polyvinyl pyrrolidone showed higher thermal stability (high Tm) and higher percentage folding reversibility in solution state (as demonstrated by solution DSC) compared to commercial, as received, and dried proteins with methacrylic acid polymer.

CONCLUSION: Polyvinyl pyrrolidone maintained the integrities and biological activities of the two model proteins not only during stresses applied by spray drying and freeze drying but also after storage of the prepared dried proteins at high conditions of RH and temperature.

Biography

Amal Ali Elkordy is a Senior Lecturer in Pharmaceutics in the Department of Pharmacy, Health and Well-being. Her area of research interest is the stabilisation of protein formulations (using spray drying and crystallisation technology) and their delivery via oral and pulmonary routes. Her work in this field has been recognised by the award of two prizes at the British Pharmaceutical Conference in 2002 and in 2004.

Her more recent work is concerned with the enhancement of poorly water soluble drugs, resulting in the award of two prizes at the British Pharmaceutical Conference 2008 and at the British Pharmaceutical Students' Association Annual Conference 2010. She also has research interests in:

- Gene therapeutics (awarded national recognition from the College of Mental Health Pharmacists, 2010)
- Liposomal drug delivery and preparation of drug eluting stents for the treatment of restenosis.

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