

Overcoming Zinc Deficiency in Children: An Assessment of Zinc Permeation across Buccal Mucosa

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INTRODUCTION: Zinc is an important mineral found to be associated with about 300 enzymes, 2000 transcriptional factors and 10% of the human proteome contain zinc-binding motives. An estimated 31% of world's population suffers from zinc deficiency with higher prevalence is observed in people with less proportion of animal products in the diet as well as the presence of phytic acid in main sources of food which inhibits zinc absorption [1]. It is estimated that about half a million deaths per year in infants and children under 5 years of age are associated with zinc deficiency [2]. Currently zinc is being administered orally, however there is evidence to suggest that oral administration results in poor absorption with bioavailability range between 14-60%. Numerous approaches, such as fortification of food and the development of inorganic, organic and chelated forms of zinc, have failed to overcome poor oral absorption. Hence the current research is proposing an alternative route of zinc administration via buccal mucosa. The buccal mucosa is part of the oral transmucosal site for drug delivery, which has great potential to deliver drug due to its ability to avoid gastrointestinal and hepatic metabolism which often limits the bioavailability of various drugs [3]. This research aimed to assess the physicochemical characteristics of different zinc salts and their effects on the permeation of zinc across buccal mucosa.

MATERIALS AND METHODS: All glassware used in the experiments were acid-washed using 4% nitric acid as per validated protocol to remove any metal impurities. Thermodynamic solubility of three zinc salts (Zinc acetate dihydrate, Zinc citrate dihydrate and Zinc sulphate monohydrate) was measured in triplicate at $37 \pm 0.5^\circ\text{C}$ in screw cap vials in three different mediums (De-ionised water, simulated saliva pH 7.4 and 0.1 M HCl). Porcine cheeks were sourced from a local supplier (Medical Meat Supplies, UK) and the buccal mucosa were prepared using a scalpel blade and trimmed appropriately to get a uniform thickness. Permeation studies were carried out using a vertical Franz diffusion cells at 37°C using 1 mL of saturated solution of different zinc salts prepared in simulated saliva as donor fluid while 10 mL of 2% nitric acid was used as receiver fluid to ensure the sink conditions. Samples were withdrawn and replaced with equal volume of receiver fluid at the pre-determined time intervals, filtered using $0.45 \mu\text{m}$ nylon syringe filter and appropriately diluted with ICP grade 2% nitric acid for analysis of zinc. Zinc was analysed in solutions using an Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES) at wavelengths of 202.548 nm, 206.200 nm, 213.857 nm, and 334.502 nm against calibration standards (5-30 ppm, R^2 : 0.999).

RESULTS AND DISCUSSION: Thermodynamic solubility results (Figure 1, Left) revealed that zinc sulphate had a relatively higher solubility in de-ionised water (206.6 mg/mL) and in 0.1M HCl (209.7 mg/mL) compared to the other salts, especially zinc citrate ($P < 0.05$), and the results correlates well with literature reports [1]. However, in simulated saliva all three salts showed low solubility, with the highest being citrate (0.58 mg/mL), followed by sulphate (0.27 mg/mL) and acetate (0.04 mg/mL). This indicates potential interactions between liberated free zinc ions on solubilisation and the components used to prepare simulated saliva (Na_2HPO_4). One possibility could be the formation of insoluble zinc phosphate complex because zinc acetate showed lowest solubility in simulated saliva although having a low stability constant ($\log K_1$: 1.03) and higher solubility (206 mg/mL) in de-ionised water compared to zinc citrate that has higher stability constant ($\log K_1$: 4.8) and low solubility (1.15 mg/mL). [4, 5]. Permeation of zinc (Figure 1, right) across buccal mucosa from zinc sulphate was significantly higher compared to other zinc salts ($P < 0.05$). It appears that zinc permeates via passive diffusion with molecular volume (MV) being dominating factor over concentration gradient as zinc citrate (MV: 143.54) although being relatively more soluble in saliva showed relatively poor permeation compared to zinc sulphate (MV: 54.62); however further investigation of using interaction-free media as donor fluids and varying degrees of saturation of zinc salts in donor media may be required to affirm this preliminary finding.

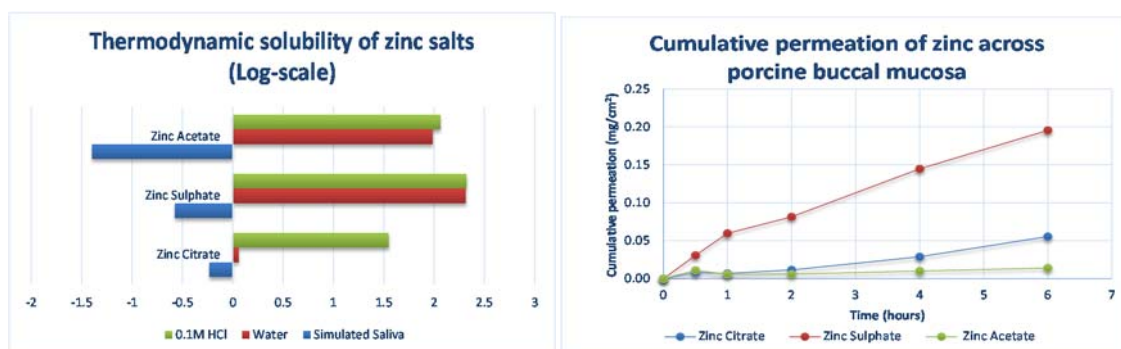


Figure 1. Solubility profile of zinc salts (left) and permeation of zinc (right) across porcine buccal mucosa (n=3)

CONCLUSION: This study showed zinc's ability to permeate across buccal mucosa and this alternative route of zinc administration could prove beneficial and has potential to open up new avenues in maximising zinc's bioavailability.

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