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BUCCAL DRUG DELIVERY OF INSULIN IN DIABETES MELLITUS : AN ATTRACTIVE ALTERNATE TO OVERCOME IN SUBCUTANEOUS ROUTE

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***Abstract*:** Buccal drug delivery of insulin is an exciting area in research and development in the field of diabetology. Buccal administration involves placing a drug between your gums and cheek where it also dissolves and also absorbed into your blood, i. e, sprays, tablets, films, etc. It is easy way to administered insulin through buccal route in pediatrics and geriatrics patients to overcome subcutaneous route.

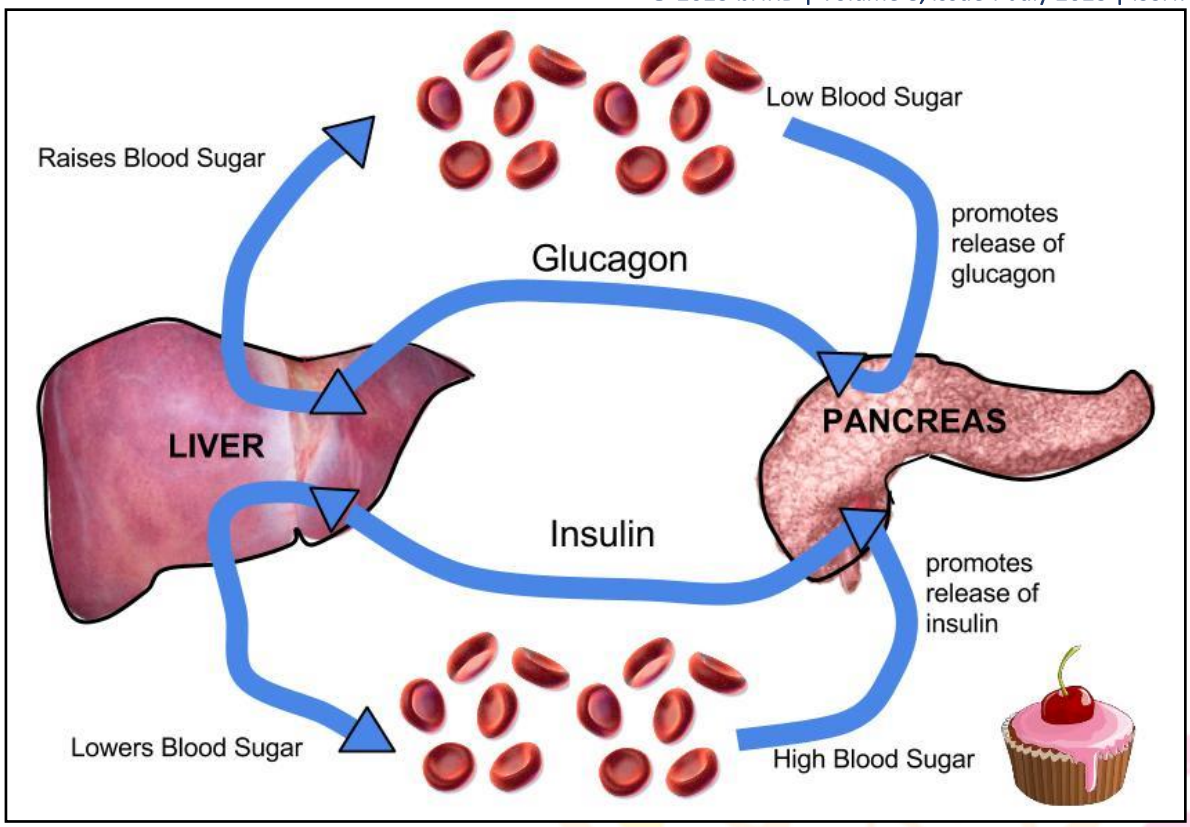
Keywords: Buccal route, Insulin, Diabetes Mellitus.

INTRODUCTION*:* Diabetes is a common condition that affects people of all ages. There are several forms of diabetes. Type 2 is the most common. A combination of treatment strategies can help you manage the condition to live a healthy life and prevent complications. Diabetes is a condition that happens when your blood sugar (glucose) is too high. It develops when your pancreas doesn't make enough insulin or any at all, or when your body isn't responding to the effects of insulin properly. Diabetes affects people of all ages. Most forms of diabetes are chronic (lifelong), and all forms are manageable with medications and/or lifestyle changes. Glucose (sugar) mainly comes from carbohydrates in your food and drinks. It's your body's go-to source of energy. Your blood carries glucose to all your body's cells to use for energy.

There are several types of diabetes. The most common forms include:
• Type 2 diabetes: With this type, your body doesn't make enough insulin and/or your body's cells don't respond normally to the insulin (insulin resistance). This is the most common type of diabetes. It mainly affects adults, but children can have it as well.

Insulin-related physiology

After it is secreted from pancreatic B-cells into the portal vein, insulin is directly transferred to the liver where it is subjected to the hepatic first-pass effect where almost half of the polypeptide hormone experiences hepatic degradation. Such an environment creates an insulin concentration gradient between hepatic portal and systemic circulation, where the liver is exposed to insulin concentration twofold to fourfold higher than that observed in the peripheral systemic circulation. Available insulin preparations fail to mimic the endogenous insulin pathway where the injectable insulin analogues are delivered directly to the peripheral circulation, hence reversing the insulin concentration gradient in normal physiology.

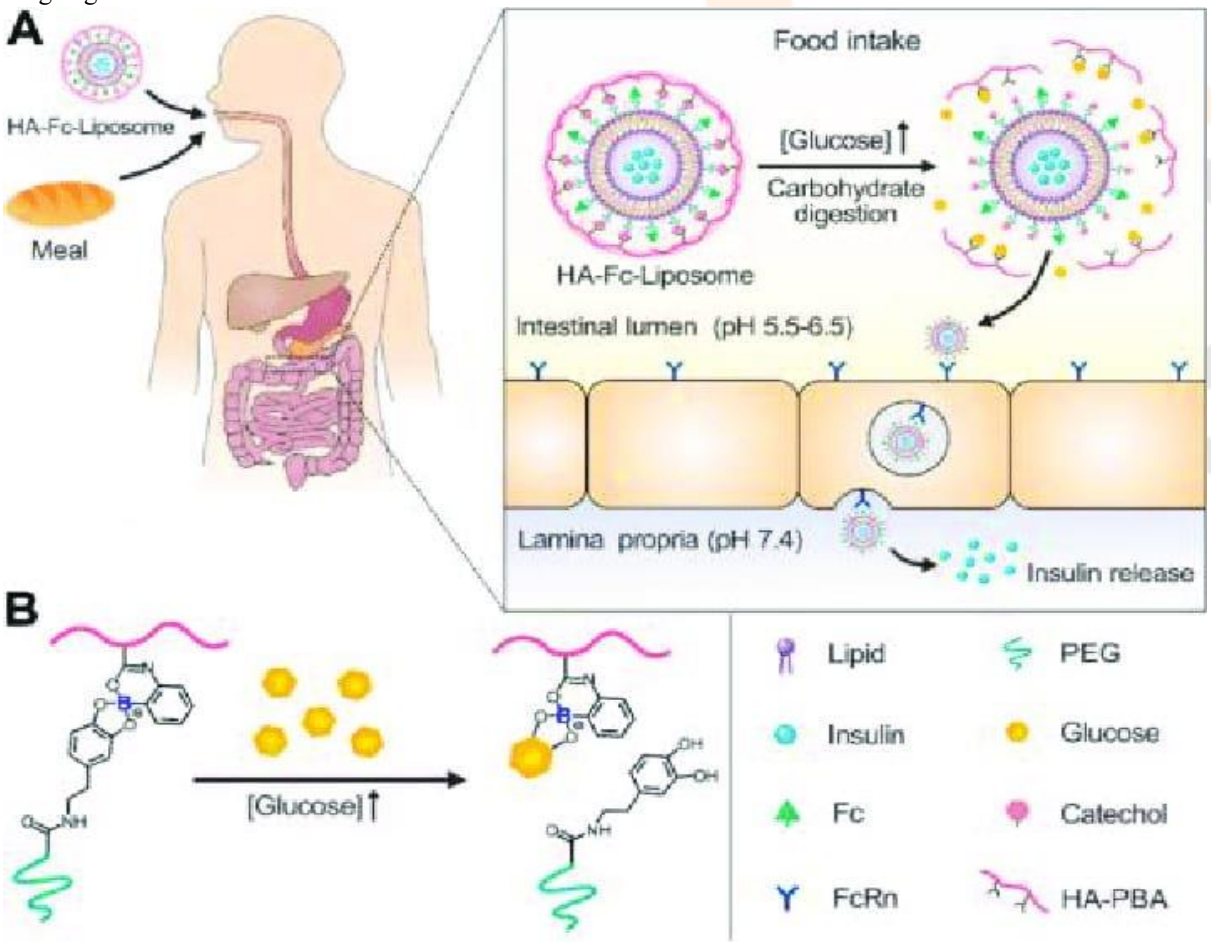


Regulation of blood glucose

Buccal as a vehicle for drug administration:

What is buccal delivery system for insulin?

Insulin reaching the systemic circulation by absorption through buccal mucosa is known as buccal insulin. Transport through the buccal mucosa is either transcellular or paracellular. Insulin traverses the epithelium via paracellular route. The buccal route provides systemic bioavailability due to the high total blood circulation through the cheek and it avoids first- pass hepatic metabolism and gastrointestinal drug degradation.



Schematic presentation of buccal administration of Insulin

Greater Tendency to Buccal Infections:
Patients with diabetes are more prone to develop infections and abscesses in the oral cavity which can in turn impair glycemic control. The susceptibility to buccal infections, like candidiasis, is favored by the presence of hyperglycemia, lower salivary flow and alterations in the composition of saliva, through modifications in its content of antimicrobial proteins like lactoferrin, lysozyme and lactoperoxidase. Buccal and oropharyngeal candidiasis is one of the most frequent opportunistic infections found in patients with impaired immunological resistance that tends to be present mostly in poorly controlled diabetic patients.

Correlation of salivary glucose level with blood glucose level:

Methodology:

A cross-sectional study was conducted in 120 patients, who were categorized as 40 controlled diabetics, 40 uncontrolled diabetics and 40 healthy, age and sex matched individuals constituted the controls. The blood and unstimulated saliva samples were collected from the patients at the different intervals for fasting, random and postprandial levels. These samples were then subjected for analysis of glucose in blood and saliva using glucose oxidase/peroxidase reagent in HITACHI 902(R) Automatic analyzer, and the results were recorded.
Results: The mean SGLS were higher in uncontrolled and controlled diabetic groups than in non-diabetic group. A highly statistically significant correlation was found between fasting salivary glucose and fasting blood glucose in all the groups.
Conclusion: With increase in BGL, increase in SGL was observed in patients with diabetes suggesting that SGL can be used for monitoring glycemic level in Diabetes Mellitus.

Advantage of buccal route of administration of insulin –

- Pre-systemic metabolism in the GI and liver is avoided, avoids first pass metabolism.
- good accessibility.
- the drug is in direct contact with the mucosa, avoiding loss in any other liquid, allowing establishment of a high drug concentration gradient across the mucosa favoring drug diffusion into the underlying tissue.
- possibility to localize the drug according to the permeability features of the target area.
- relatively large surface for absorption (100-200 cm^2).
- level of vascularization is very high in some areas.
- weak variations of pH.
- The convenient route and painless administration, facility to modulate the selection of excipients, versatility in the design of multidirectional or unidirectional release systems for local or systemic action, and a predictable drug concentration in the blood.

Drawbacks of buccal route of administration of Insulin –

- the buccal mucosa is not an absorptive organ (intestinal mucosa). Its structural histological and biochemical features are those of a lining but not absorptive mucosa (pluri-stratified epithelium and intercellular barrier of permeability), thus promoting absorption from the buccal mucosa is a challenge by definition.
- there exist great variations of permeability among the different areas of the oral mucosa.
- sublingual area is thin and nonkeratinized, highly permeable (high drug input).
- cheek mucosa is thicker and nonkeratinized, fairly permeable (low but sustained drug input).

Result: When Insulin administered buccal route, then there is presence of more blood vessels direct absorption of insulin into blood takes place. so, avoid first pass metabolism. So, reduce the peptide degradation in the GI. So, due to buccal route of Insulin administration decrease in blood glucose level.

Conclusion: As administered Insulin through buccal route then reduce blood glucose level.

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