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Formulation and Evaluation of Hydrogel containing Arginine for dentine Hypersensitivity

Monika Dubey* **and Praveen Kumar Jain**
VNS group of Institutions, Faculty of Pharmacy, Bhopal, (MP) - India

Abstract

Dentine hypersensitivity is a common problem found in many adult populations. Around 57% world population is suffering from this problem. The commonest teeth affected are the premolars. Dentine hypersensitivity peaked between 40 and 50 yrs of age, followed by decline with age. The purpose of this study was to evaluate the protective action of arginine against the cavaties formed in enamel. For this purpose, hydrogels, contining arginine were formulated and then after evaluating its several parameters, in vivo study was also performed in lower and upper cannines of helthy rats and results were quite satisfactory, when compared with control groups.

Key-Words: Hypersentivity, Hydrogel, Arginine

Introduction

Dentine hypersensitivity is defined as short, sharp pain arising from exposed dentine typically in response to chemical, thermal or osmotic stimuli that cannot be explained as arising from any other form of dental defect. Mature enamel is a crystalline structure, containing up to 96% inorganic material by weight; primarily a carbonate-containing form of calcium hydroxyl apatite. The remainder of the enamel is made up of around 3% water and 1% organic matter including proteins and lipids. The average size of the crystallites is about 30 nm thick by 6 and translucent and the true colour shows mainly at the cutting edges of the tooth. Where the enamel is 10 nm wide and several microns long although size may vary with depth. Enamel is white thinner, the darker underlying dentine may show through.

Causes: Dentine is a calcified tissue which is generally covered by enamel in a tooth crown and by a protective layer called cementum in the tooth root. It contains many of microscopic tubular structures that radiate outwards from the pulp.Enamel can be lost as a result of aggressive or incorrect tooth brushing, over consumption of acidic food and tooth grinding caused by stress and par functional behavior. When the root of the tooth is exposed to the mouth due to the gum recession, the cementum covering the tooth root can easily be removed and dentine is exposed resulting in dentine hypersensitivity.[1-3]

*** Corresponding Author**
E.mail: mdb.0405@gmail.com,
praveen_jain782002@yahoo.com

Symptoms/signs of Dentine Hypersensitivit

Pale yellow colour, Spacing between teeths, Open pores on enamel**,** Blackening of gums**,** Bleeding from gums, Pain occur in cold or hot drinks.

Hydrodynamic theory of Dentine Hypersensitivity

It suggest that changes in the flow of the fluid present in the dentinal tubules can trigger receptors present on nerves located at the pulpal aspect, there by eliciting a pain response. This hydrodynamic flow can be increased by changes in temperature, pressure, humidity and osmotic pressure or forces acting onto the tooth. If the occlusion of tubules is only superficial daily tooth brushing, saliva or consumption of acidic beverages may easily open the dentine tubules.

Hydrogels are three dimensional, hydrophilic, polymeric networks capable of imbibing large amount of water or biological fluids, defined as a material that exhibits the ability to swell in water and retain a significant fraction of water with in its structure. There is a wide variety of natural and synthetic hydrogels. Their ability to absorb water is due to the presence of hydrophilic groups. Hydrogels are used pharmaceutically as lubricants and as carriers for spermicidal agents and other drugs for their local effect and percutaneous absorption. Hydrogel can be applied directly to the wounded area and once daily application of the gel had proved to be satisfactory in removing offensive odor emanating from such wound. A hydrogel is a semisolid system of at least two interpenetrating phases: a gelling agent and a liquid. Gels that contain water are called hydrogels, while that contain an organic liquid are called organogels.

Hydrogels in the broad sense include the matrix of water soluble materials such as cellulose derivatives and natural gums. These pseudohydrogels swell infinetly and the component molecules dissolve from the surface of the molecules. Drug molecules are released through the spaces in the network and also by the dissolution and disintegration of the matrix. Muccoadhesive polymers of natural semisynthetic or synthetic origin are able to form hydrogels. In the simplest case the drug is dispersed in the muccoadhesive polymer which swells in the presence of water and exhibit bioadhesive properties.

A hydrogel can be defined as a material that exhibits the ability to swell in water and retain a significant fraction of water with in its structure. There is a wide variety of natural and synthetic hydrogels. Their ability to absorb water is due to the presence of hydrophilic groups.

Hydrogels have attracted tremendous research interest over many years, in part for fundamental reasons and in part because of the potential for a wide range of applications. Hydrogels have been successfully used in biomedical fields due to their high water content and the consequent biocompatibility. Successful examples include soft contact lenses, wound dressing, superabsorbent, and drug-delivery systems.[2-5]

Objectives

Hydrogels form to easy the application, to overcome the drawback of other formulation. The molecular weight, sequence, and even higher order structures of these biopolymers can be precisely controlled to levels that remain unsurpassed. Biologically functional moieties such as that enhancing cell adhesion can be readily incorporated. The synthesis process does not involve toxic monomers as chemical polymerization does. In contrast to naturally derived polymers, the structure and properties of genetically engineered biomaterials can be systematically varied, providing engineering flexibility. These artificial protein hydrogels have promise for many biomedical applications.

Control of physical and biological properties of these hydrogels is essential for their biomedical applications. It has been shown that rigidity of materials acts as an extracellular signal and plays a critical role in regulating cell adhesion, spreading, migration, and even survival.

Material and Methods[6-12]

Preformulation studies

Organoleptic properties

The organoleptic property of drug like colour and odour was evaluated by the process described above.

Melting Point

Melting point of arginine was determined by Melting Point apparatus. A small quantity of arginine was taken in a capillary tube and the tube was fitted in the melting point apparatus and the point at which sample started to melt was recorded as its melting point.

Solubility Studies

Solubility of arginine in different solvents was studied in different solvents like water, methanol, ethanol, phosphate buffer.

Preparation Of Phosphate buffer, pH 7.4

2.38 g of disodium hydrogen phosphate, 8g of Sodium chloride and 19 g of potassium dihydrogen phosphate was dissolved in distill water and volume was made upto 1000ml.

Colorimetric estimation of arginine

A solution of nynhydrin was prepared by dissolving 2 gm of nynhydrin in 25 ml of acetone. Added to this Solution, 25 ml aof acetate buffer pH 5.5. stored in brown bottle to protect from light.

Method of preparation of acetate buffer , pH 5.5:272 gm of sodium acetate was dissolved in 500 ml of water at 35º C and added 50 ml of glacial acetic acid and volume made up by sufficient water.

Preparation of Calibration Curve In Phosphate Buffer pH 7.4

100 mg of arginine was dissolved in 100ml of phosphate buffer pH 7.4. 10 ml of above stock was diluted to 100ml with phosphate buffer pH 7.4. Dilutions in concentration range of 2- 20 µg/ml were prepared.

Preparation Of Calibration Curve In water

100 mg of arginine was dissolved in 100 ml of distilled water. 10ml of above stock solution was diluted to 100ml with . Dilutions in concentration range of 2-20 µg/ml were prepared.

Fourier Transform Infrared Spectroscopy

FTIR of pure drug arginine and carbopol 934 was performed to determine the purity of the drug and to detect any possible interaction between arginine and carbopol 934.

Method of preparation of hydrogel

Prepared a solution of polymer in water in a ratio of 99:1,Then prepared another solution of drug in water. Added drug solution slowly in the polymer solution with continuous stirring. Then added calcium carbonate, preservative, permeation enhancer and saccharin into it. Then heated it at 70 ºC for 1 hour.

Evaluation of hydrogel

The prepared hydrogels were evaluated for physical appearance, spreadibility, pH, drug content, in vitro and in vivo study.

Table 1: Formulation Design

Content	Formulation I	Formulation II	Formulation III	Formulation IV	Formulation V
Arginine	8g	8g	8g	8g	8g
Calcium carbonate	1g	1g	1g	1g	1g
Carbopol 934	1g	1.4g	1.8g	2.2g	2.6g
Propylene glycol	2ml	2ml	2ml	2ml	2ml
Methyl paraben	0.05mg	0.05mg	0.05mg	0.05mg	0.05mg
Propyl paraben	0.05mg	0.05mg	0.05mg	0.05mg	0.05mg
Saccharin	5mg	5mg	5mg	5mg	5mg

Results and Discussion

The organoleptic properties of the formulation were shown below:

Table 2: Organoletic properties of Arginine

Drug	Test	Specification	Observation
Arginine	Colour	White fine powder	White fine powder
	Odour	Odourless	Odourless

The melting point was found to be 232-240.

Table 3: Melting Point of Arginine

Drug	Reported Melting Point	Observed Melting Point
Arginine	220-244	232-240

Solubility of arginine in different solvents was studied in different solvents like water, methanol, ethanol, phosphate buffer.

Table 4: Solubility of Arginine

Solvents	Solubility
Water	Highly soluble
Ether	Insoluble
Alcohol	Sparingly soluble

Calibration curve of Arginine were recorded in distilled water and phosphate buffer and were presented in Fig. 1.

The prepared hydrogels were evaluated and the results were shown in table 5.

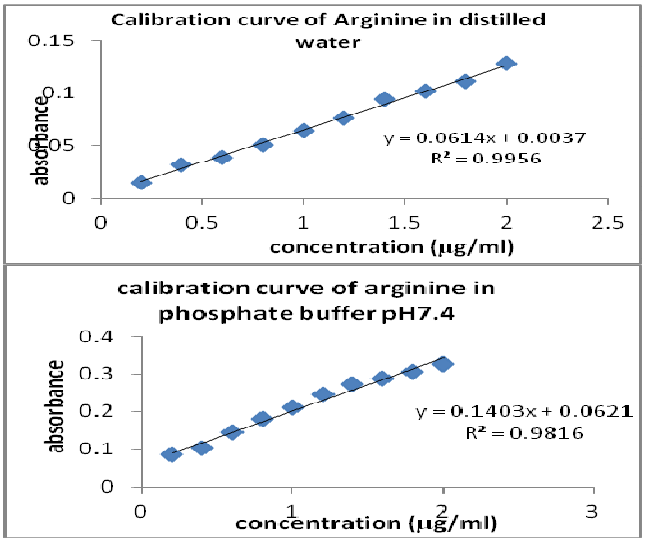

Fig. 1: Calibration Curve of Arginine

Table 5: Evaluation of Hydrogel

Parameters	F 1	F 2	F 3	F 4	F 5
Colour	White	White	White	White	White
Odour	Aggreable	Aggreable	Aggreable	Aggreable	Aggreable
Homogeneity	Yes	Yes	Yes	Yes	Yes
viscosity	17780 ± 458.257	33350 ± 1387.743	25200 ± 655.743	59333 ± 832.66	71040 ± 557.494
swelling	34.15 ± 4.207	46.32 ± 2.206	43.04 5 ± 5.098	60.9 ± 2.064	56.2± 2.969
Spreadi	54.44	61.94	59.04	54.44	59.11

bility (g.cm/sec)	± 2.696	± 3.0203	± 12.807	± 3.365	± 3.654
pH	6.9 ± 0.62	7.0 ± 0.2	7.4 ± 0.43	7.63 ± 0.41	7.7± 0.30
Drug Content (1 ml)	.00693	.00693	.00127	.00149	.0007
Drug Content (in 30ml)	.020	.020	.038	.044	.021

Values are expressed in Mean±SD

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