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Formulation and Development of Cetirizine Hydrochloride Nasal Solution as Intranasal Drug Delivery System

Gadakh Pravin Pandharinath[1], Sarangdevot Yuvrajsing[1], Ram Nema[1], Jadhav Khanderao R.[2]*, Bachhav R. S.[2] and Jadhav Sujit A.[2]

[1]B.N. Pharmacy College, Udaipur, Rajasthan, India
[2]R.G. Sapkal College of Pharmacy, Nashik, Maharashtra, India

**Corresponding Author*

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Abstract: The Intranasal Delivery is preferable route for administration of the drug for local, systemic as well as central nervous system. Advantages of intranasal spray dosage form is that it is cost-effective, easy to use/carry and self-administrable. High patient compliance make this dosage form growing opportunity for intranasal drug delivery. Extensive bioavailability is achieved by intranasal drug delivery system. It avoids first pass metabolism and thereby achieves high therapeutic effect and less toxic effect. This article outlined the formulation development of Cetirizine Hydrochloride intranasal solution. Pre-formulation study and formulation of cetirizine HCl was performed which showed rapid drug diffusion. It is intuitively expected that this study will help to understand intranasal formulation and it's *in vitro* characteristics. Cetirizine is an antihistaminic used to relieve allergy symptoms such as watery eyes, runny nose, hives and itching. It works by blocking histaminic receptors which is responsible for allergic reaction. Cetirizine solution help to get relieves allergic symptoms related to rhinitis.

Keywords: Intranasal solution, Intranasal drug delivery system, Formulation, *In vitro* characterization

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Introduction

Intranasal drug delivery is recognized to be a useful and reliable alternative to oral and parenteral routes. The intranasal route of drug delivery can be used for both local and systemic drug delivery. For instance, localized intranasal drug delivery is usually used to treat conditions related to the intranasal cavity, such as congestion, rhinitis, sinusitis and related allergic conditions. A diverse range of drugs including corticosteroids, anti-histamines, anti-cholinergic and vasoconstrictors can be administered locally. In recent years, achieving a systemic drug action using the

Table 1: Human Epithelial Characteristics

Nasal Section	Epithelial cells/Functions	Surface area	Vacuolization	Permeability
Vestibule	Stratified Squamous Keratinized and epithelial cells with nasal hairs/ supports and protection	0.6 cm^2	Low	Poor
Atrium	Stratified Squamous cells/ supports pseudostratified cells/ supports	NF	Low	Reduced
Respiratory Region	Columnar non-ciliated cells/ support - Columnar ciliated cells/ support and mucialary clearance - Globet cells/Mucus secretion -Basal cells/other progenitor other cells types	130 cm^2	Very high	Good
Olfactory Region	Sustentacular cells/ support and synthetic - Olfactory receptor cells/ olfaction perceptions - Basal cells/ Progenitors of other cell types	15 cm^2	High	Direct access to CNs

nose as the entry portal into the body has received more attention. Also, the intranasal delivery seems to be a favourable way to circumvent the obstacles for blood brain barrier (BBB) allowing the direct drug delivery in the bio phase of central nervous system (CNS)-active compounds. It has also been considered to the administration of vaccines. Now a day's multiple types of formulation are used to administer drug by intranasal route, which includes Intra-nasal spray, intranasal drop, intranasal powder, intranasal gels and intranasal insert etc. Administration of drugs through the nose in the spray dosage form is a non-invasive method that gives rapid onset of drug action. Because the Intra-nasals spray dosage form is cost-effective, easy to use/carry and self-administrable, it has high patient compliance. Therefore, intranasal drug delivery has become a popular route of drug administration and has strong growth opportunity.

The present study outlines the properties of drugs and formulation characteristics that determine decisively the pharmacokinetics of intranasal preparations (Table 1). Cetirizine sold under the brand name Zyrtec among others, is a second-generation antihistamine used to treat allergic rhinitis (hay fever), dermatitis, and urticaria (hives). It is taken by mouth (Djupesland, 2013). Effects generally begin within an hour and last for about a day. The degree of benefit is similar to other antihistamines such as diphenhydramine.

The medication common side effects include sleepiness, dry mouth, headache, and abdominal pain. The degree of sleepiness that occurs is generally less than with first generation antihistamines. Use in pregnancy appears safe, but use during breastfeeding is not recommended. It works by blocking histamine H_1 receptors, mostly outside the brain.

The present study aimed to formulate and develop Cetirizine hydrochloride nasal solution and to evaluate Cetirizine hydrochloride nasal solution for intra-nasal delivery system.

Materials and Methods

Drug (Cetirizine) sample was evaluated for colour and texture. The melting point of cetirizine HCl as 100 -115 °C was determined by taking a small amount of sample in a capillary tube closed at one end and placed in melting point apparatus. The melting point was estimated in triplicate. The

Table 2: Absorbance data with different concentration

Concentration (ppm)	Absorbance
10	0.587
20	0.694
30	1.004
40	1.200
50	1.346
60	1.573

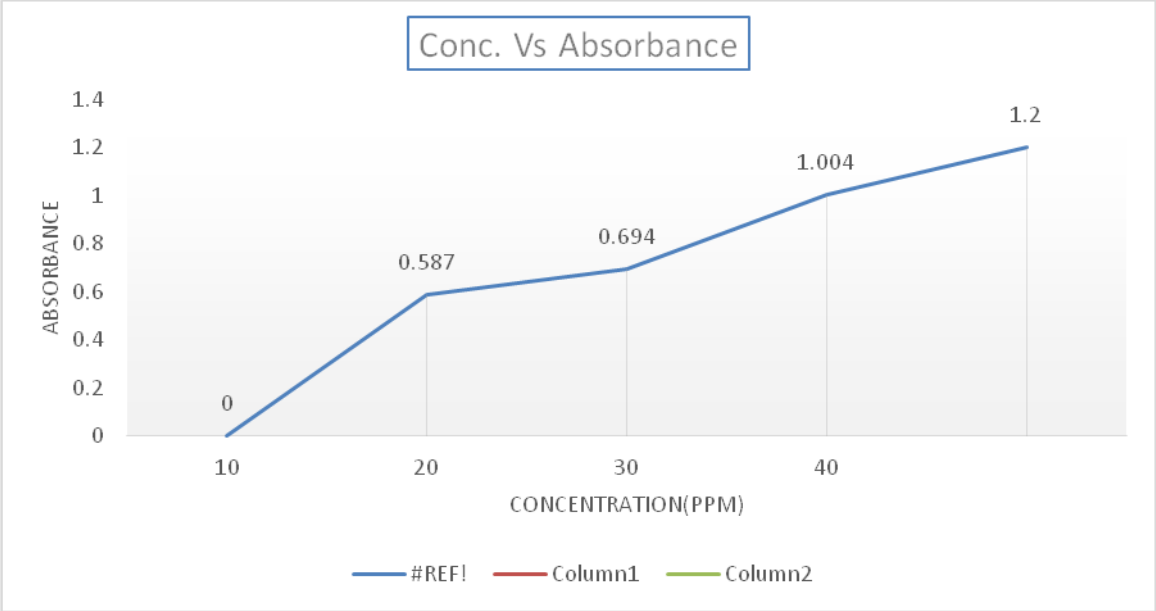

Fig.1: Calibration Curve of Cetirizine hydrochloride in water.

solubility of cetirizine HCl was checked in different solvents like distilled water, methanol, DMSO and ethanol.

Calibration curve of cetirizine HCl by UV visible spectroscopy:

The UV spectrum of cetirizine HCl was obtained by using Ultraviolet Spectrophotometer. Accurately weighed 10 mg of the drug was dissolved in sufficient quantity of water and volume was made up to 100 ml to obtain a concentration of 100 µg/ml. 1 ml of the aliquot was withdrawn and volume was made up to 10 ml using water to obtain the concentration of 10 µg/ml. The resultant solutions were scanned from 200-400 nm and the spectrum was recorded to obtain the value of maximum wavelength (Table 2; Fig. 1).

Formulation and development of intranasal solution:

The quantities of drug and other ingredients were weighed as per formula shown in Table 3 and formulation were prepared in following manner:

- Cetirizine solution was prepared by simple mixing method.
- All the glasswares were washed with distilled water
- Took distilled water in beaker and added sodium chloride in water and stirred it well till it get dissolved completely.

Table.3: Master formulation of Cetirizine HCL intranasal solution

Component	Concentration	Role in formulation
Sodium chloride	0.9%	Tonicity adjustment
Cetirizine HCL	2mg	API
Sodium lauryl sulphate	1-2%	Surfactant
EDTA	1-5%	Cation chelating agent
Carboxyl methyl cellulose	0.1-1%	Suspending agent
Polyethylene glycol	0-5%	Co -Solvent
Glycerin	Less than 30%	Humectant
Sodium hydroxide	Q.S.	PH Adjustment

Table 4: Readings of Viscosity

Spindle no.	S62
Viscosity	18 cp
RPM	15
Temperature	28.1 ℃

- Added cetirizine hydrochloride anddissolved well till a clear solution was obtained.
- Added Polyethylene glycol as a co-solvent to dissolve undissolved moiety.
- Added EDTA 1-5% as a chelating agent and added sodium lauryl sulphate 1%.
- Added CMC and Glycerin serially to develop viscosity of solution.
- At the end added NaOH to adjust the pH 6.5.
- Stirred all the ingredients carefully to get clear solution and evaluated it for further parameters.

Evaluation Parameters:

Clarity: The clarity of the solution was measured by visual inspection under black and white background.

pH: pH of each formulation was determined by using Digital pH meter. pH of solution was found to be 6.5. The pH values were recorded immediately after preparation.

Viscosity: The viscosity was determined by the Brookfield Viscometer; type DV-II+PRO using spindle no. LV 3(63). Viscosities of the formulations were taken at two different temperatures i.e. at room temperature and at 37 °C with varying shear rate. Dimension of the study is shown in Table 4.

Diffusion study:

1. The intranasal mucosa of Goat shown in Figure 2 was separated from sub layer bony tissues. After the complete removal of blood from mucosal surface, it is attached to donor chamber tube.
2. The donor chamber tube is placed in such a way that it just touches.The diffusion medium is recipient chamber.
3. At predetermined intervals, sample (0.5 ml) from recipient chamber was withdrawn and transferred to amber-colored ampoules.
4. The samples withdrawn was suitably replaced. The samples were estimated for drug content by suitable analytical technique.
5. Temperature was maintained at 37℃.

Results and Discussion

Intranasal delivery is the logical choice for topical treatment of local diseases in the nose and para-

Table 5: % Cumulative drug release from Diffusion Study

Time (min)	% Cumulative Drug Release
0	0
5	10.50
10	25.23
15	44.50
20	58.61
25	64.48
30	78.10
40	99.70

intranasal sinuses such as allergic and non-allergic rhinitis and sinusitis. The nose is also considered an attractive route for needle-free vaccination and for systemic drug delivery, especially when rapid absorption and effect are desired. In addition, intranasal delivery may help address issues related to poor bioavailability, slow absorption, drug degradation, and adverse events in the gastrointestinal tract and avoids the first-pass metabolism in the liver.

Cetirizine is white amorphous powder and soluble in water. Cetirizine melting point was found as 112 ℃. Result of calibration curve is shown in Table 1. The solution was found to be clear under dark background. The pH was found to be 6.5. The viscosity of solution was found to be 18 CP. Diffusion study of Cetirizine HCl solution showed 99.70 % diffusion from mucosal membrane within 60 min (Table 5).

Intranasal administration therapy also called "Nasya karma" was mostly used form of treatment in the past and accepted in Ayurvedic system of Indian medicines. The early 1980s saw the introduction of intranasal route as a promising systemic delivery alternative to the other conventional drug delivery route (Putheti *et al*., 2009; Rahisuddin *et al*., 2011). Intranasal route is easily accessible, convenient, and a reliable with a porous endothelial membrane and a highly vascularized epithelium that provides a rapid absorption of compounds into the systemic circulation, avoiding the hepatic first pass elimination. In addition, intranasal drug delivery enables dose reduction, rapid attainment of therapeutic blood levels, quicker onset of pharmacological activity, and fewer side effects (Behl *et al.*, 1998; Pagar *et al*., 2013).

The intranasal cavity is mainly used for treatment of local diseases of the upper respiratory tract such as intranasal congestion, intranasal infections and intranasal allergic diseases e.g. allergic rhinitis. Cetirizine is a second-generation antihistamine used to treat allergic rhinitis (hay fever), dermatitis, and urticaria (hives).

It is taken by mouth and the effects generally starts within an hour and last for about a day. The medication Common side effects include sleepiness, dry mouth, headache, and abdominal pain. The degree of sleepiness that occurs is generally less than with first generation antihistamines. Use in pregnancy appears safe, but use during breastfeeding is not recommended. It works by blocking histamine H_1 receptors, mostly outside the brain.

Conclusion

The nose is attractive for delivery of many drugs and vaccines, but the potential has not been fully realized. Inherent challenges related to the intranasal anatomy, physiology and aerodynamics that may severely limit the potential and clinical efficiency are not widely understood. The small and dynamic dimensions of the intranasal cavity and the anterior anatomy are among the most

important hurdles for more efficient intranasal drug delivery. Considering the potential benefits from intranasal route of administration, we should expect to see a range of novel intranasal products reaching the market in the near future. They will include not only drugs for local treatment but also for systemic protection against infections. The development of drugs directly target the brain in order to attain a good therapeutic effect in CNS with reduced systemic side effects. Intranasal drug delivery can be affected by several factors e.g. biological factors, physiological factors, physicochemical properties of drugs, physicochemical properties of formulation. Intranasal solution of Cetirizine hydrochloride was formulated and evaluated as Intranasal drug delivery.

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