Formulation And Evaluation of Taste Masked Granules of Drotaverine Hcl

Neelesh Kushwaha[1], Dr Reetesh Yadav[2], Dr Deepak Patel[3], Dilend Patle[4]
[1,4]*Shri Ram Institute of Pharmacy Jabalpur, Madhya Pradesh, India*
[2,3]*Assistant Professor, Shri Ram Institute of Pharmacy Jabalpur, Madhya Pradesh, India*

***Abstract*—Drotaverine hydrochloride is an antispasmodic drug widely used in the treatment of gastrointestinal and genitourinary disorders. However, its intensely bitter taste can lead to poor patient compliance, especially in pediatric and geriatric populations. The present study was aimed at the formulation and evaluation of taste-masked granules of drotaverine hydrochloride to improve palatability and acceptability. Taste masking was achieved by preparing granules using suitable polymers through an appropriate granulation technique. The prepared granules were evaluated for micromeritic properties, drug content, taste masking efficiency, and in-vitro drug release. Taste evaluation studies indicated a significant reduction in bitterness compared to the pure drug. In-vitro dissolution studies demonstrated that the optimized formulation released the drug rapidly in gastric conditions without affecting its therapeutic performance. The results of the study confirmed that effective taste masking of drotaverine hydrochloride was successfully achieved, leading to improved patient compliance and suitability for oral administration.**

***Index Terms*—Drotaverine hydrochloride; Taste masking; Granules; Patient compliance; Oral drug delivery system**

I. INTRODUCTION

Oral drug delivery is the most widely employed route of drug administration due to its convenience, non-invasiveness, ease of self-medication, and high patient acceptance. However, the success of an oral formulation depends not only on its pharmacological efficacy but also on its palatability. The taste of drugs is a major determinant of patient compliance, particularly in pediatric and geriatric populations, who are highly sensitive to bitter or unpleasant tastes. Poor taste can result in reduced adherence, incomplete dosing, and compromised therapeutic outcomes, highlighting the importance of taste masking in oral drug delivery.

Drotaverine hydrochloride is a spasmolytic drug widely used for the management of smooth muscle spasms in the gastrointestinal, biliary, and genitourinary tracts. Despite its potent antispasmodic activity, drotaverine hydrochloride is intensely bitter, which limits its acceptability, particularly in liquid formulations, orally disintegrating tablets, or chewable dosage forms. Consequently, there is a critical need to develop strategies to mask its unpleasant taste while ensuring that the drug's therapeutic efficacy is preserved.

Taste masking of bitter drugs can be achieved through various approaches, such as polymer coating, microencapsulation, complexation, adsorption onto inert carriers, and granulation-based techniques. Among these, taste-masked granules have gained particular attention due to their simplicity, cost-effectiveness, and scalability. Granulation-based taste masking offers several advantages, including uniform drug distribution, ease of handling, protection of the drug from the taste buds, rapid drug release in the gastric environment, and compatibility with multiple oral dosage forms, such as suspensions, sachets, and tablets.

In addition to improving palatability, taste-masked granules can also enhance the stability and flow properties of the drug, making them suitable for further formulation into solid dosage forms. Optimizing the choice of polymer or carrier and the granulation technique is essential to achieve effective taste masking without compromising drug release.

The present study focuses on the formulation and evaluation of taste-masked granules of drotaverine hydrochloride using suitable polymers and granulation techniques. The primary objectives were to reduce the bitterness of drotaverine hydrochloride, maintain rapid and complete drug release under gastric conditions, and improve overall patient compliance. This research aims to provide a practical approach to producing palatable, effective oral formulations of bitter drugs, thereby enhancing their therapeutic acceptability and clinical performance.

II. MATERIALS AND METHODS

Materials

Drotaverine hydrochloride – Active pharmaceutical ingredient (API)

Polymer for taste masking – Hydroxypropyl methylcellulose (HPMC), Lactose microcrystalline cellulose (MCC) – Diluent

Magnesium stearate – Lubricant

Talc – Glidant

Solvents – Purified water, ethanol (for wet granulation if required)

All chemicals and reagents used were of pharmaceutical or analytical grade.

Methods

1. Preparation of Taste-Masked Granules

Taste-masked granules of drotaverine hydrochloride were prepared using either wet granulation or coacervation/adsorption-based granulation techniques depending on the selected polymer.

Procedure

Drotaverine hydrochloride and polymer were weighed accurately in required ratios.

The drug and polymer were mixed with the diluent lactose to form a uniform dry blend.

A small volume of solvent ethanol was added gradually to prepare a damp mass suitable for granulation.

The damp mass was passed through a sieve #20 to form granules.

Granules were dried in a hot air oven at 40–50°C until a constant weight was achieved.

Dried granules were passed through a sieve #40 to obtain uniform size.

Finally, magnesium stearate (1–2% w/w) and talc (1% w/w) were added as lubricant and glidant and blended uniformly.

Alternative method:

In some formulations, adsorption or polymer coating techniques were used, where the drug was coated with the taste-masking polymer to reduce bitterness without affecting drug release.

III. EVALUATION OF GRANULES

The prepared granules were evaluated for the following parameters:

3.1. Micromeritic Properties

Angle of repose – to assess flow properties

Bulk density and tapped density – to calculate compressibility

Carr's index and Hausner ratio – to evaluate flowability

3.2. Drug Content Uniformity

Granules were powdered, dissolved in a suitable solvent, filtered, and analyzed spectrophotometrically at the λmax of drotaverine hydrochloride to determine drug content.

3.3. Taste Masking Efficiency

Taste evaluation was conducted using a human sensory panel or an electronic tongue.

Bitterness reduction was assessed by comparing the taste-masked granules with pure drug.

3.4. In-Vitro Drug Release Study

Dissolution studies were performed using USP Type II (paddle apparatus).

Granules were placed in 900 mL of 0.1 N HCl (pH 1.2) at 37 ± 0.5°C and stirred at 50 rpm.

Samples were withdrawn at predetermined intervals, filtered, and analyzed spectrophotometrically.

Optimized formulations were stored under accelerated conditions (40°C ± 2°C, 75% RH ± 5%) for 3 months.

Samples were evaluated for drug content, taste, and in-vitro release.

IV. RESULTS AND DISCUSSION

Table 1.1: Cumulative percent drug release dvs.time from ODT prepared with drotaverine HCl-Compritol melt granules (mean±s.d., n=3)

In vitro dissolution studies

Time (min)	CP7	CP8	CP9	CP10	CP11
5	22.23±0.78	35.00±0.55	52.47±0.56	29.12±0.34	40.91±0.34
10	53.26±0.88	54.43±0.28	69.53±0.23	47.54±0.23	60.21±0.55
15	69.06±0.99	70.12±0.76	75.91±0.78	63.12±0.86	72.93±0.78
20	76.02±1.34	79.12±1.45	82.11±1.23	72.23±1.56	79.11±1.55
30	82.12±1.14	83.23±1.77	88.12±1.46	81.54±1.49	
45	91.12±1.23	89.99±1.35	99.43±1.66	88.32±1.60	91.11±1.77
60	100.01±1.02	98.12±1.29	99.99±1.79	94.12±1.87	99.98±1.56
75		100.11±1.02		100.09±1.33	

DSC analysis

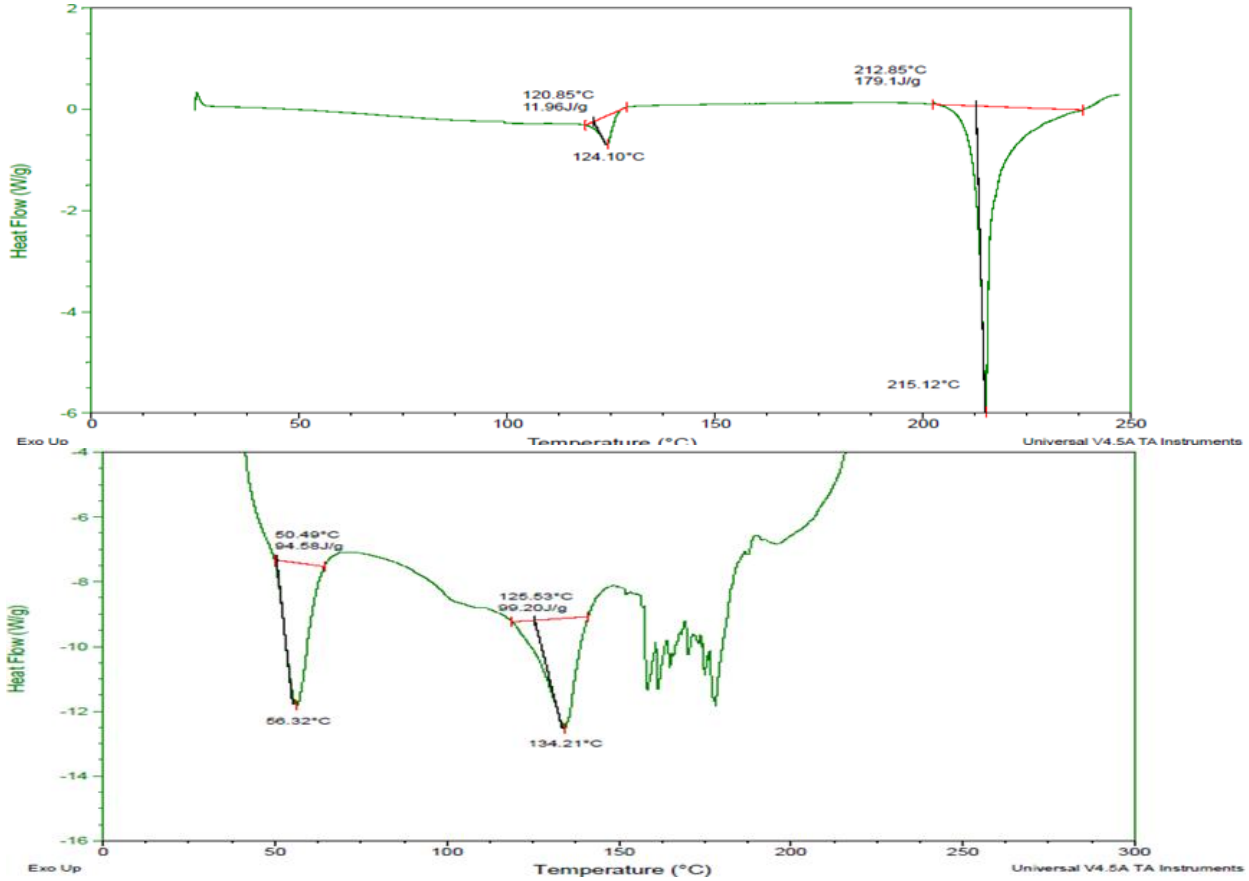


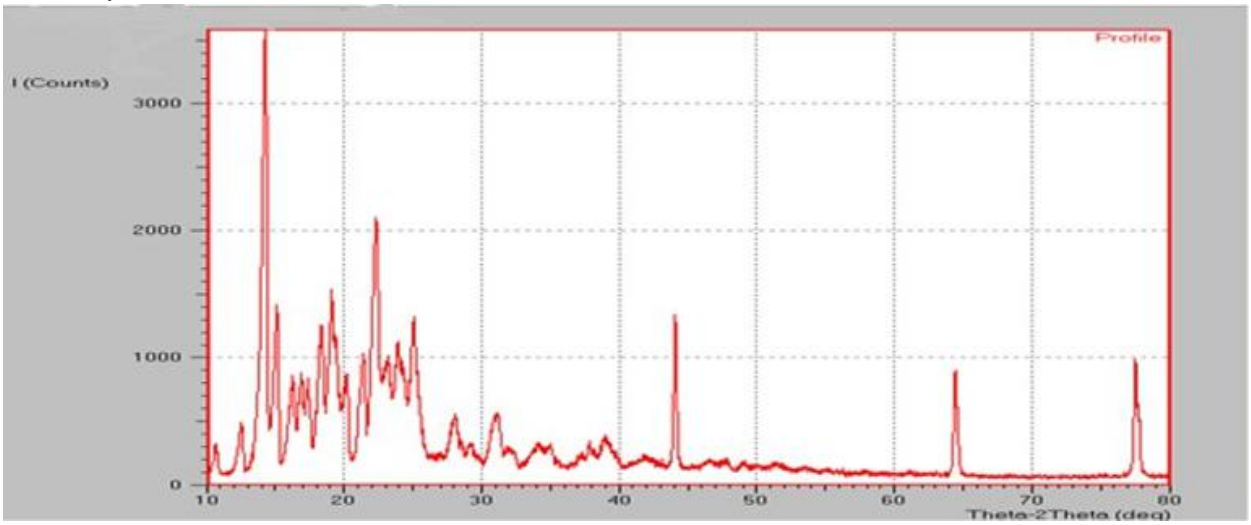
Fig.1.1: DSC thermograms of a) DrotaverineHCl b) H9 tablet

The DSC thermograms of pure drug and optimized formulation are shown in Fig. 1.1. The DSC thermogram of pure drotaverine HCl exhibited a sharp endothermic peak at 215.12° C corresponding to its melting point, indicating its crystalline nature.

There is a shift in the melting peak of drotaverine HCl in the optimized formulations H9 to 56.32ºC and

134.21ºC. The shift observed in the melting peak of drotaverine HCl in the optimized formulation may be due to physical interaction between the drug and excipient. Compared to pure drug the melting peak was broadened to some extent in the formulation which may be due to changes in its crystalline form. The low melting point of the excipients might have influenced the shift in the melting point of the drug in the formulation.

XRD analysis:



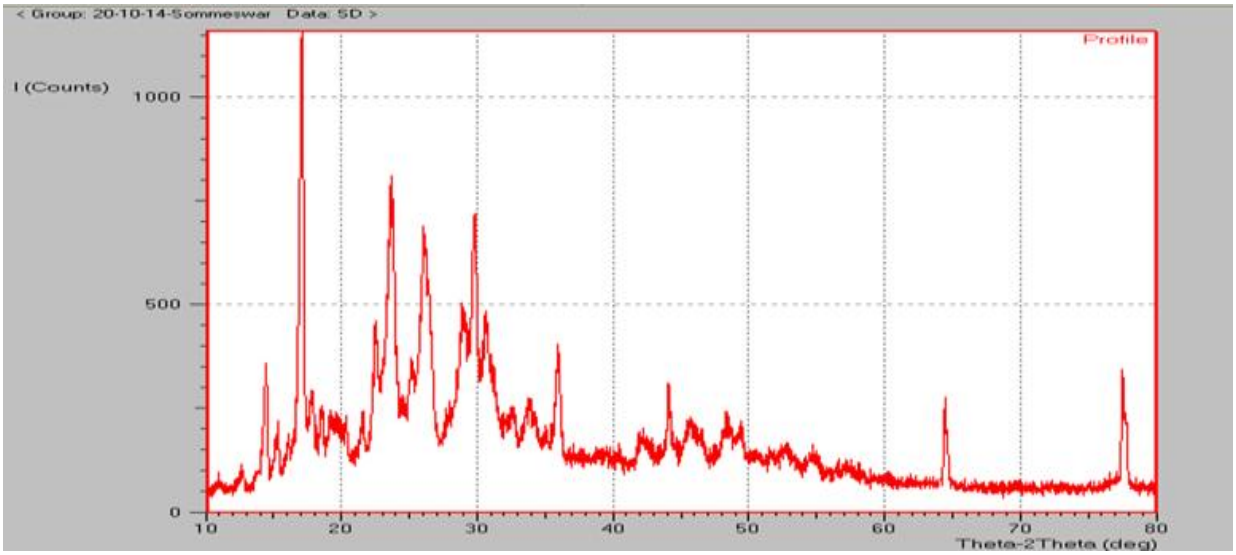


Fig.1.2:X-raydiffractograms of a) Drotaverine HCl, b) Formulation H9

The X-ray diffractograms of pure drug drotaverine HCl and optimized formulation are shown in Fig. 1.2. XRD diffractograms for pure drug and formulation were studied for comparison. The diffractogram of drotaverine HCl showed characteristic sharp intensity diffraction peaks at 2 values of 14.5, 22, 44, 65 and 77, which reflected the crystalline nature of drug. The optimized formulation H9 showeddiffractionpeaksatrespective2□valuesofpuredrotaverine

HCl although the irrelative intensities were reduced, suggesting reduced degree of crystallinity of drug in these formulations.

Fourier Transform Infrared Spectroscopy:

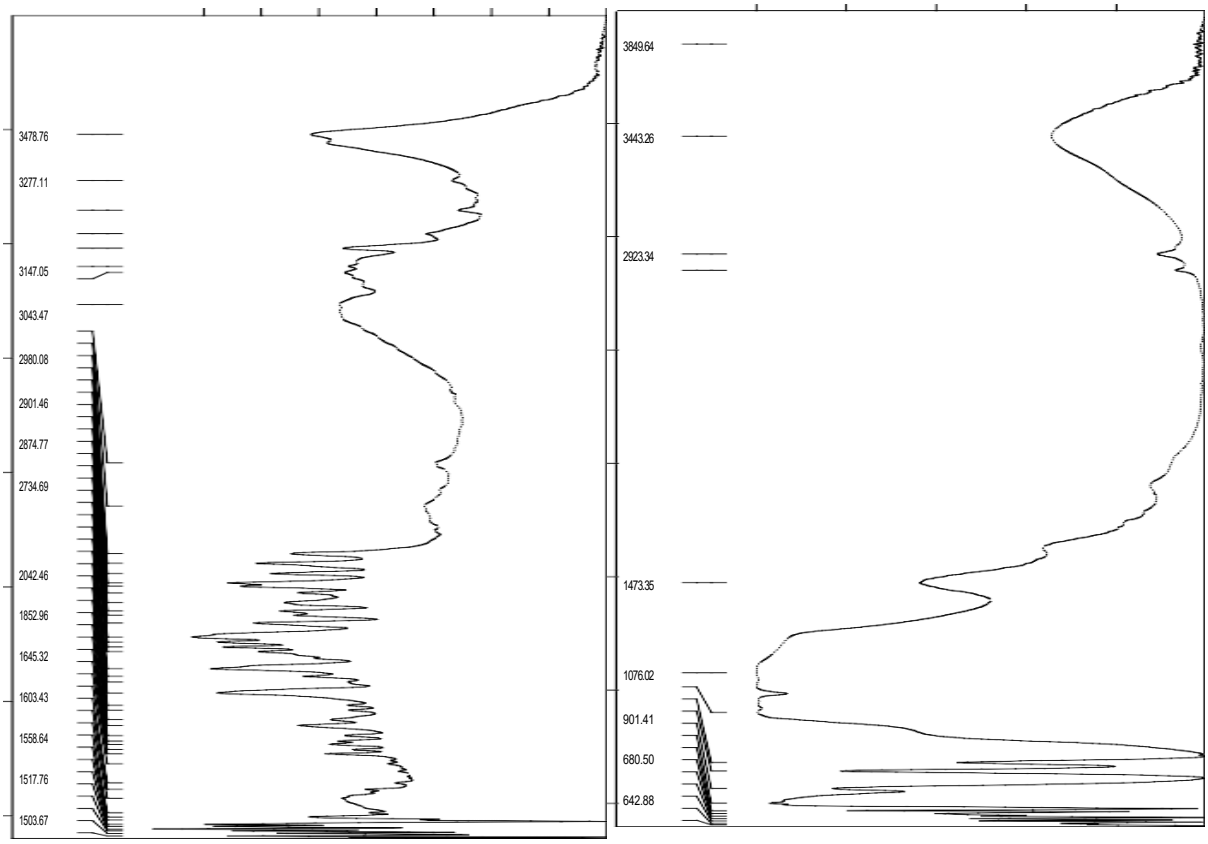


Fig.1.3: FTIR spectra of a) DrotaverineHCl b) Rxcipient

V. CONCLUSION

As there are no reports on the development of taste-masked dosage forms for drotaverine HCl by using HPMC (3 cps) and excipient, an attempt was made to prepare taste-masked ODT of drotaverine.

Drug-carrier solid mixtures of HPMC and excipient were prepared by the kneading method. The ratio of drug-carrier solid mixture was confirmed by evaluation of taste and mouth feel by human volunteers, and it was found that the taste of the drug was masked at 1:7.5 for the recipient and 1:9 for HPMC. These polymers coat the drug so that the bitterness of the drug may not be felt. The order of taste-masking ability of the carriers when judged by human volunteers was found to be HPMC > Rxipient.
The drug-carrier solid mixture granules were compressed into tablets with different super disintegrants like crospovidone, croscarmellose sodium, and sodium starch glycolate, sweetener aspartame, and mannitol by the wet granulation method with excipient and the direct compression method for HPMC formulations.
The prepared tablets were evaluated for tableting parameters and found to be satisfactory. The in vitro dissolution studies for all the formulations were performed, and it was observed that the formulations R10 and H9 have shown maximum drug release in 60 min; therefore, they are better formulations when compared with MF.

From DSC, XRD, and FTIR studies, no chemical changes in the drug with changes in crystallinity of the drug were observed. To conclude, this study showed that HPMC and Rxcipient can be suitably used for taste masking of drotaverine HCl. HPMC was found to be a better taste-masking agent when compared to the recipient.

Thus, the objective of preparing taste-masked ODT of drotaverine HCl was achieved with solid mixtures using Rxipient and HPMC 3.

REFERENCES

[1] USP30-NF25. The official compendia of standards. The United States Pharmacopoeia Convention. Powder flow. (e-book). 2007, 643.
[2] Tran D. “Some aspects of the property of angle of repose of powders.” Journal of Pharmacy and Pharmacology, 1, 127-135, 1957.
[3] USP30-NF25. The official compendia of standards. The United States Pharmacopoeial Convention. Bulk Density and Tapped Density (e-book). 2007, 242.
[4] CraickDJ. “The flow properties of starch powder sand mixtures.” Journal of Pharmacy and Pharmacology, 10, 10, 1958.
[5] Indian Pharmacopoeia. Govt of India, Ministry of Health and Family Welfare, the Indian Pharmacopeia Commission, Ghaziabad, India. 2010, I, 187-193.
[6] Sivaprasad Reddy S, Hindustan Abdul Ahad, Sreenivasulu R, Kishore Kumar Reddy, Krishna Mahesh Ch, Kranthi G, and Chandrasekhar. “Novel approach in designing mouth-dissolving tablets for bitter drugs, taking clozapine as a model drug.” Der Pharmacia Lettre, 3(1), 113-120, 2011.
[7] BiYX, Sunada H, Yonezawa Y, and Danzo K. “Evaluation of rapidly disintegrating tablets.” Drug Development and Industrial Pharmacy, 25, 571-581, 1999.
[8] Subrahmanian S, Sankar V, and Asha Asokan Manakadan. “Formulation and evaluation of cetirizine dihydrochloride orodispersible tablet.” Pakistan Journal of Pharmaceutical Sciences, 23(2), 232-235, 2010.
[9] Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, and Piccerelle P. “Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration.” International Journal of Pharmaceutics, 292, 29–41, 2005.
[10] Uchida T, Nakamura T, Tanigake A. “The effect of various substances on the suppression of the bitterness of quinine—human gustatory sensation, binding, and taste sensor studies.” Chemical and Pharmaceutical Bulletin (Tokyo), 50, 1589-1593, 2002.
[11] Eri Katsuno, Kohei Tahara, Yoshiko Takeuchi, and Hirofumi Takeuchi. “Orally disintegrating tablets prepared by a co-processed mixture of micronized crospovidone and mannitol using a ball mill to improve compatibility and tablet stability.” Powder Technology, 241, 60–66, 2013.