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Pharmaceutical Sciences **RESEARCH ARTICLE ……!!!**

FORMULATION AND EVALUATION OF NABUMETONE BUCCAL TABLETS

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KEYWORDS:

Bioadhesion, mucoadhesion, nabumetone, buccal, tablets.

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ABSTRACT

Mucoadhesive drug delivery systems interact with the mucus layer covering the mucosal epithelial surface, and mucin molecules and increase the residence time of the dosage form at the site of absorption. Mucoadhesion while considering drug delivery is having several merits, because of the ideal physiochemical characters of the mucosal membrane. Various sites for mucoadhesive drug delivery system are ocular, nasal, buccal cavity; GIT, vaginal, rectal and several specific dosage forms have been reported. The main aim of this work was to study mucoadhesive buccal tablets of nabumetone using various suitable bioadhesive polymers such as CP 934, HPMC K4M, and Na CMC. A backing layer of ethyl cellulose was used which is impermeable in nature. Four formulations were prepared by direct compression method. The prepared tablets were characterized by swelling studies, surface pH, bioadhesive properties, I*n-vitro* drug dissolution and *In-vitro* diffusion studies. The surface pH of all formulations was found to be satisfactory, and values were in between the range of 5.5-7 pH. The drug release was found to be zero order release. The formulation MD4 was considered as the optimized formulation based on satisfactory evaluation parameters.

INTRODUCTION:

Bioadhesion may be defined as the state in which two materials, at least one of which is biological in nature, are held together for extended period of time by interfacial forces. In pharmaceutical sciences, when the adhesive attachment is to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion[1].In the early 1980s; academic research groups working in the ophthalmic field pioneered the concept of mucoadhesion as a new strategy to improve the efficacy of various drug delivery systems. Since then, the potential of mucoadhesive polymers was shown in ocular, nasal, vagina and buccal drug delivery systems leading to a significantly prolonged residence time of sustained release delivery systems on this mucosal membranes[2-5]. In addition, the development of oral mucoadhesive delivery systems was always of great interest as delivery systems capable of adhering to certain gastrointestinal (GI) segments would offer various advantages. With few exceptions, however, mucoadhesive drug delivery systems have so far not reached their full potential in oral drug delivery, because the adhesion of drug delivery systems in the GI tract is in most cases insufficient to provide a prolonged residence time of delivery systems in the stomach or small intestine[6-8]. The need to deliver 'challenging' molecules such as biopharmaceuticals (proteins and oligonucleotides) has increased interest in this area. Mucoadhesive materials could also be used as therapeutic agents in their own right, to coat and protect damaged tissues (gastric ulcers or lesions of the oral mucosa) or to act as lubricating agents (in the oral cavity, eye and vagina).

Materials and methods:

Materials

Nabumetone was obtained as a gift sample from Sidmac Pharmaceuticals ltd. Dehradun. All other chemicals and reagents used were of analytical grade and quality.

Methods

A) Preparation of standard curve of nabumetone:

Standard plot of nabumetone was prepared in 6.8 pH. Nabumetone was dissolved in 50 ml of phosphate buffer to produce primary stock solution having a concentration of 1 mg/ml. 0.5-3 ml aliquots of the secondary stock were diluted to 10 ml to produce standard solutions having concentrations of 5-30 µg/ml. The absorbance of the solutions was measured at 259 nm using double beam UV-Visible spectrophotometer. The plot of absorbance vs. concentration (µg/ml) was plotted and data was subjected to linear regression analysis.

B) Preparation of mucoadhesive buccal tablets:

Tablets were prepared by direct compression technique. The ingredients of core layer of different

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combinations were accurately weighed and mixed in a glass mortar and pestle for 30 min to obtain uniform mixture. The mixture was passed through 60 µm mesh. Then core layer of the above mixture was compressed at minimum compaction force in 10 mm punches of single stroke tableting machine. The upper punch was raised without disturbing the core tablet and impermeable backing layer Ethyl cellulose of 40 mg was weighed and added on core tablet and again compressed using optimum compression force.

TABLE NO. 1 Formulations

Ingredients (mg)	**MD1**	**MD2**	**MD3**	**MD4**
Nabumetone	20	20	20	20
Carbopol	40	--	20	--
Hpmc k4m	--	40	20	40
Sod. Cmc	20	20	20	20
Mcc	30	30	30	30
Mag. Stearate	q.s	q.s	q.s	q.s
Talc	q.s	q.s	q.s	q.s
Ethyl cellulose	50	50	50	50

C) Evaluation parameters:

The following evaluation parameters were performed

- Powder flow properties
- Friability
- Hardness
- Weight variation
- Content uniformity
- Swelling index
- Surface pH
- *Ex-vivo* mucoadhesion strength- By using modified balance apparatus in goat mucosa
- *In-vitro* dissolution
- *In-vitro permeation study*- By using Franz diffusion cell and goat mucosa

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RESULTS AND DISCUSSION

Results:

a) calibration curve of nabumetone:

FIG. NO. 1 Standard curve of Nabumetone

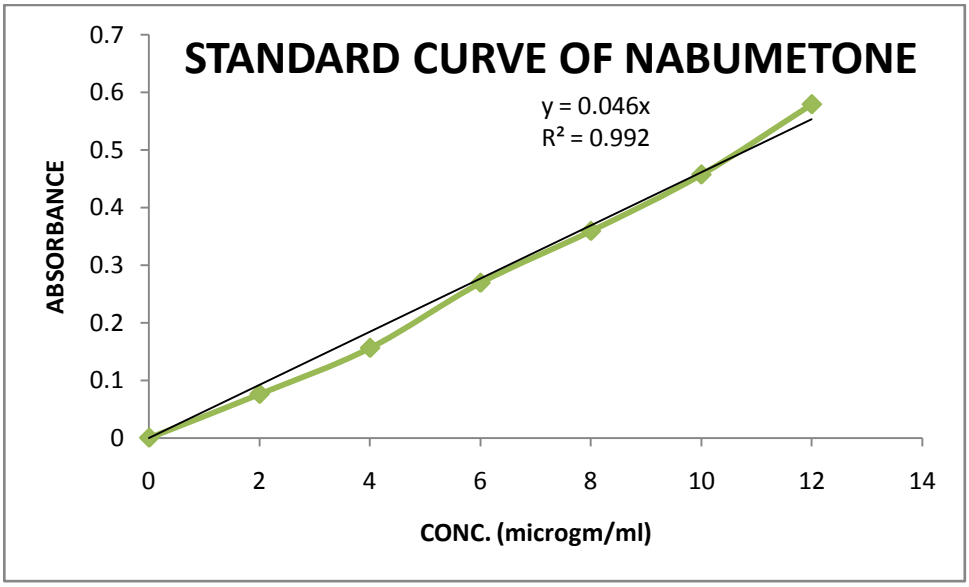

TABLE NO. 2 Evaluation Parameters

FORMULATION	HARDNESS (kg/cm^2)	FRIABILITY	WEIGHT VARIATION	CONTENT UNIFORMITY	SURFACE Ph
MD1	5.4	0.54%	3.5%	92.45%	5.7
MD2	5.7	0.67%	3.7%	89.56%	6.2
MD3	5.6	0.76%	4.5%	91.4%	6.5
MD4	5.9	0.43%	2.3%	94.6%	6.7

Table no. 3 Mucoadhesive Parameters

FORMULATION	BIOADHESIVE TIME (HOURS)	BIOADHESIVE STRENGTH (GRAMS)
MD1	6.23	20.56
MD2	6.57	24.5
MD3	7.2	29.7
MD4	6.9	25.6

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Fig no. 2 Hardness

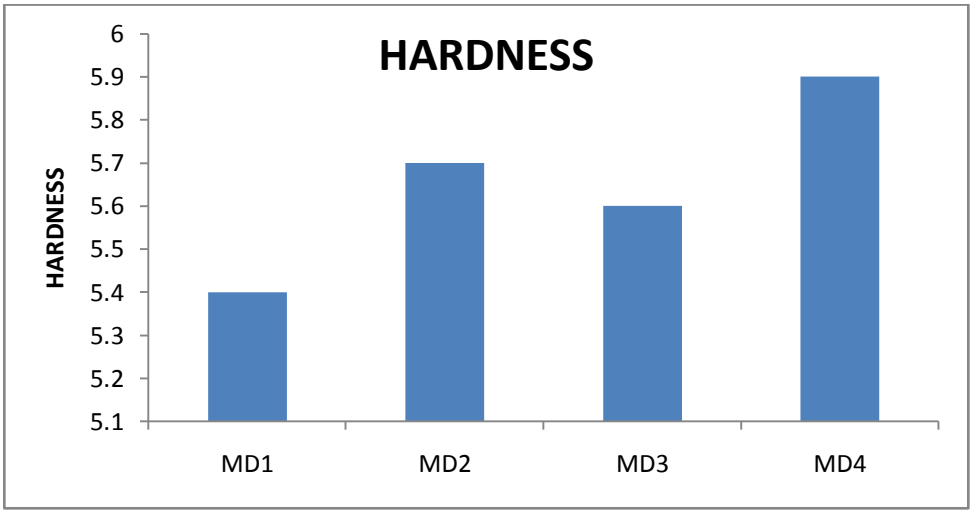

Fig. no. 3 % Friability

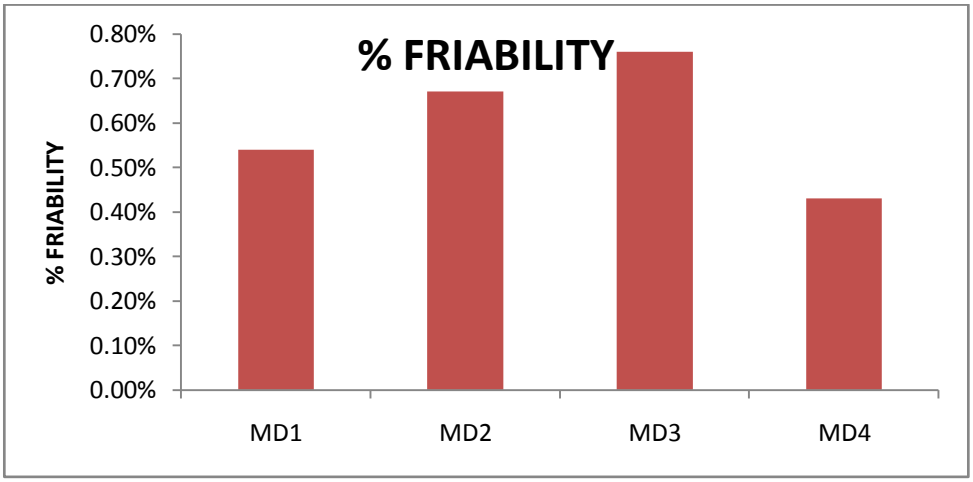

Fig. no. 4 % Drug Content

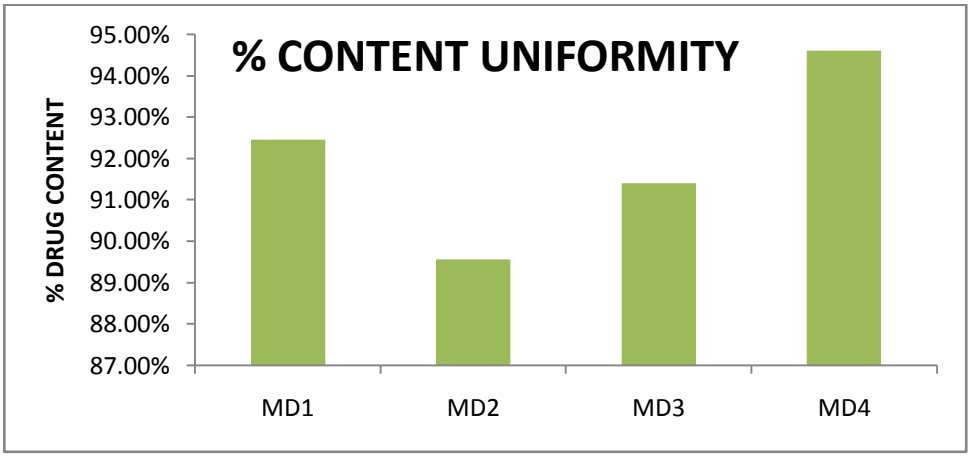

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Fig. no. 5 % Weight Variation

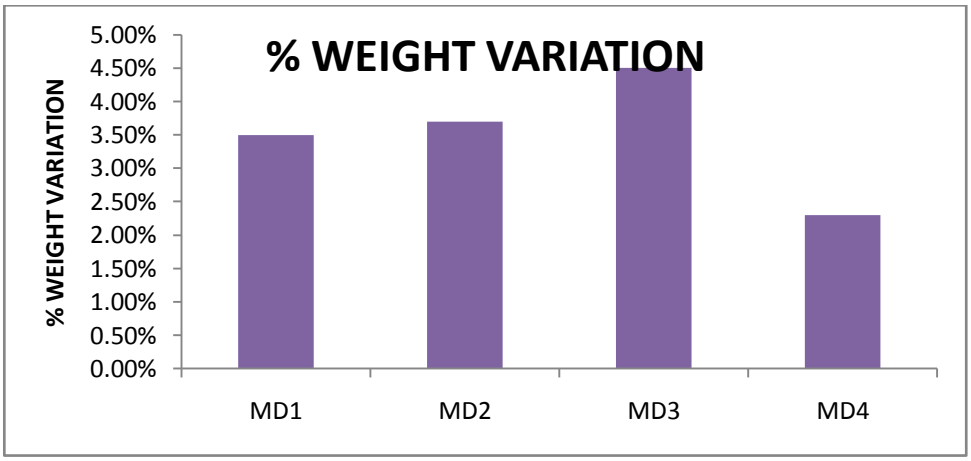

Fig no. 6 Surface pH

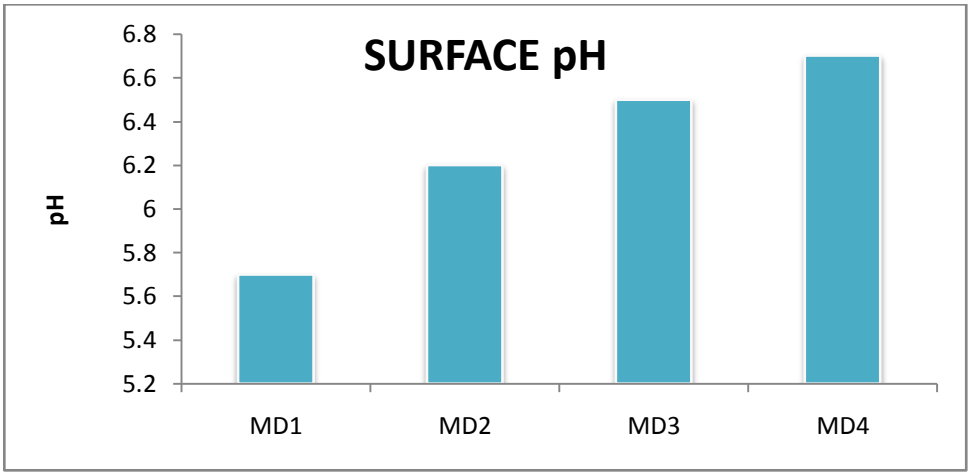

Fig. no. 7 Mucoadhesive properties

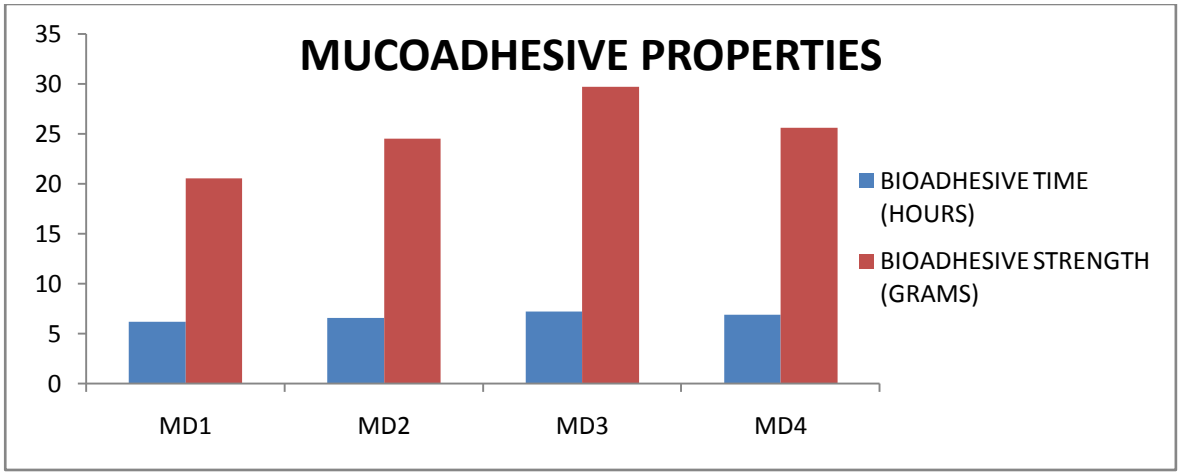

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Fig no. 8 *% In Vitro* dissolution study

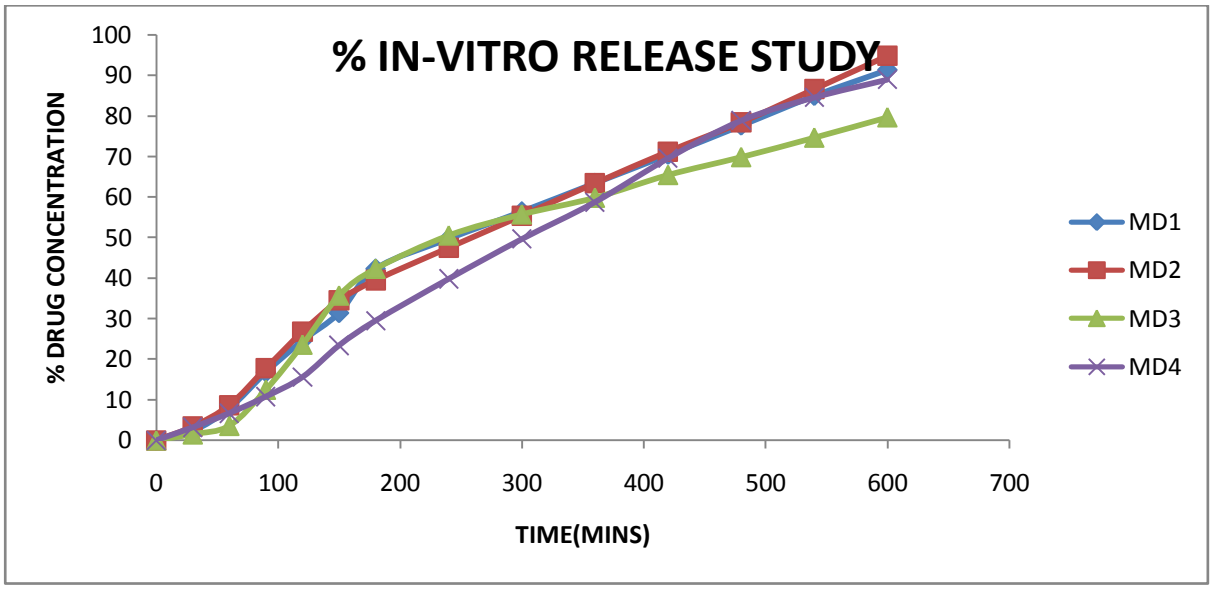

Table no. 4 kinetic data of formulation MD1

Model Fitting	R^2	K
Zero order	0.9305	0.1454
1st order	0.9370	-0.0035
Higuchi Matrix	0.9338	10.0879
Peppas	0.6008	0.9415
Hix.Crow.	0.9603	0.0008

Table no. 5 kinetic data of formulation MD2

Model Fitting	R^2	K
Zero order	0.9317	0.1466
1st order	0.8845	-0.0039
Higuchi Matrix	0.9297	10.2803
Peppas	0.6021	1.1044
Hix.Crow.	0.9395	0.0009

Table no. 6 kinetic data of formulation MD3

Model Fitting	R^2	k
Zero order	0.8642	0.1281
1st order	0.9438	-0.0025
Higuchi Matrix	0.9462	9.3280
Peppas	0.5166	0.7820
Hix.Crow.	0.9255	0.0007

Table no. 7 kinetic data of formulation MD4

Model Fitting	R^2	K
Zero order	0.9621	0.1510
1st order	0.9401	-0.0034
Higuchi Matrix	0.9371	10.2705
Peppas	0.6698	0.8299
Hix.Crow.	0.9630	0.0008

Table no. 9 comparative r^2 values

MODEL FITTING	MD1	MD2	MD3	MD4
Zero order	0.9305	0.9317	0.8642	0.9621
First order	0.9370	0.8845	0.9438	0.9401
Higuchi matrix	0.9338	0.9297	0.9462	0.9371
Peppas	0.6008	0.6021	0.5166	0.6698
Hix. Crow.	0.9603	0.9395	0.9255	0.9630

Table no. 10 best fit models

Formulation	Model
MD1	**Hixon Crowell**
MD2	**Hixon Crowell**
MD3	**Higuchi Matrix**
MD4	**Hixon Crowell**

CONCLUSION:

Nabumetone buccal tablets were successfully prepared by direct compression process. four batches were prepared, all of them showing optimum physical stability and parameters. The formulation MD3 was the optimum formulation based on evaluation parameters. It contains 1:1 ratio of HPMC: carbopol. The parameters were 5.6 kg/cm^2 hardness, 0.76% friability, 4.5% weight variation, 92% content uniformity along with 7 hours of mucoadhesion time (ex-vivo). The in-vitro release showed a $t_{50\%}$ of 6 hours and $t_{80\%}$ of 10 hours and higuchi matrix type release. Further work is to be carried out in order to determine its efficacy and safety by long term pharmacokinetic and pharmacodynamic studies in human beings.

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