ISSN: 0975-766X
Research Article
Available Online through
www.ijptonline.com

# DESIGN AND DEVELOPMENT OF BIOADHESIVE ANTIFUNGAL VAGINAL TABLET: PHYSIOCHEMICAL CHARACTERIZATION AND *IN-VITRO* EVALUATION

**Rohit Bisht[1]*, Amitava Ghosh[2]**
Siddartha Institute of Pharmacy, Dehradun, Uttrakhand.
S.G.R.R. Institute of Technology and Science, Dehradun, Uttrakhand.
*Email: rohit_thakur1234@rediffmail.com*

*Received on 14-03-2011* *Accepted on 29-03-2011*

**Abstract**

The aim of present investigation is to develop bioadhesive antifungal vaginal tablet in order to provide long term therapeutic action at the site of infection. Fluconazole is taken as a model drug. Carbopol 934, Carbopol-940, hydroxypropylmethyl cellulose (HPMC) and Guar gum were used as candidate bioadhesive polymers. Tablets are compress directly from powder blends of active ingredients and excipients. Bio adhesive vaginal tablet is prepared by direct compression method .Selected batch were incorporated in direct compression method using various grades of Bioadhesive polymer such as Carbopol-940,Carbopol-934,Hydroxypropyle Methylcellulose (H.P.M.C.) and Guar gum with other formulation additives. Micromeritic studies of powders were performed for angle of repose, Bulk density, Tapped density, compressibility index. The formulation were subjected to different evaluation parameters such as weight variation, hardness, friability, shape and size, disintegration, bioadhesive strength, swelling behavior. In-vitro drug release studies were carried using USP type II dissolution apparatus (paddle type) at 50 rpm. The data subjected to different models in order to determine the drug release mechanism.

**Key words:** Anti-fungal, Bioadhesive, Vaginal drug delivery, Micromeritic studies, Drug release.

## Introduction

The vagina, as a site for drug delivery, offers certain unique features that can be exploited in order to achieve desirable therapeutic effects. Considerable progress has been made in this research area over the past few years and, at present, the anatomy and physiology, microflora and secretions of the vagina are well understood. By contrast,

the scientific knowledge regarding the possibilities of drug delivery via the vagina is limited. To date, there are only a limited number of vaginal dosage forms (VDFs) available, although various possibilities are presently being explored. The currently available VDFs have limitations, such as leakage, messiness and low residence time, which contribute to poor subject or patient compliance. Attempts are being made to develop novel vaginal drug delivery systems (NVDDS) that can meet the clinical as well as the user's requirements. This review will focus on the various aspects, scope and potential of vaginal drug delivery.[1]

**Vaginal anatomy and physiology with reference to drug delivery**

The vagina is an important organ of the reproductive tract with a major role in reproduction, it has unique features in terms of secretion pH and microflora, and these factors must be considered during the development and evaluation of VDFs.[2,3] The vagina also has great potential for systemic delivery because of its large surface area, rich blood supply and permeability to a wide range of compounds including peptides and proteins.[4]

Fluconazole, a synthetic triazole derivative, is an azole antifungal agent. Azole antifungals interfere with fungal cytochrome P450 enzyme activity necessary for the demethylation of 14-alpha-methyl sterols to ergosterol, the principal sterol in fungal cell membranes. As ergosterol is depleted, the fungal cell membrane is damaged. Unlike ketoconazole, fluconazole has a very weak, noncompetitive inhibitory effect on the liver cytochrome P450 enzyme system, while maintaining a high affinity for fungal cytochrome P450 enzyme activity. In Candida albicans, azole antifungals inhibit transformation of blastospores into invasive mycelial form. Fluconazole has not been reported to have antiandrogenic activity at currently used doses, and does not affect cortisol metabolism in patients treated with clinically recommended doses.[5]

**Materials and Methods:**

Fluconazole was received as a gift sample from Windlass Pharmaceuticals pvt ltd. Dehradun, Uttrakhand. India. Carbopol 934, Hydroxypropyl Methylcellulose and Guar Gum were purchased from S.D. Fine Chem. Limited, Mumbai (India). All grades of kyron were purchased from COREL PHARMA CHEM, Ahmadabad (India).and

starch com. Grade (Web Research Laboratory, Mumbai) and Magnesium stearate (LR) from S.D .Fine Chem. Limited, Mumbai.

**Preparation of bioadhesive vaginal tablets:**

Tablets are compress directly from powder blends of active ingredients and excipients. Bio adhesive vaginal tablet is prepared by direct compression method .Selected batch were incorporated in direct compression method using various grades of Bioadhesive polymer such as Carbopol-940,Carbopol-934,Hydroxypropyle Methylcellulose (H.P.M.C.) and Guar gum with other formulation additives.[6]

**Evaluation of powder:**

**Flow properties**

**Measurement of angle of repose:**

The angle of repose was determined by funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (□) was calculated.

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r)$$

More cohesive material form higher heaps, which less spread are out.[7]

**Bulk density**

Apparent bulk density ($P_b$) was measured by pouring the pre-weighed (M) blend into a graduated cylinder. The bulk volume ($V_b$) of the blend was determined. Then the bulk density was calculated by using the formula.

$$\text{Bulk density } (Pb) = M/V_b$$

**Tapped density:** The measured cylinder containing a known mass (M) of blind was tapped for a fixed time, and the minimum volume (VT) occupied in the cylinder was measured. The tapped density (Pt) was calculated by using the following formula.

$$\text{Tapped density } (Pt) = M/Vt$$

**Hausner's ratio**

Hausner's ratio is an index of ease of powder or granule flow property. It was calculated by the following formulae.

**Hausner's Ratio= Tap density / Bulk Density**

The value greater than 1.25 indicates poor flow (33% Carr index) and value less than 1.25 indicates good flow (20% Carr index). If it is between 1.25-1.5 added glident normally to improve flow property. [8]

**Compressibility Index:**

**A** simple indication of ease with which a material can be induced to flow can be determined by the help of the Compressibility or Carr's index (I).

It was determined by the help of the given formulae.

**$I= (1-V/V_O)$ Where:**

**V=** The volume occupied by the granules after being subjected to a standardized tapping procedure.

**$V_O$**= the volume occupied by the granules before tapping procedure. The value below 15% indicates good flow property and value above 25% indicates poor flowability. [(3)]

**Evaluation of tablets:**

**Weight variation**

A series of 20 tablets are taken and their average weight is compared and the deviation is measured. The weight variation is the measure of the uniformity in the weight of the tablets prepared and hence uniformity of the dosage. [9]

**Hardness**

In pharmaceutical industry the mechanical strength is referred to as the crushing strength or the hardness .Hardness of the tablets is dependent on the binding efficacy of the binder. In the common apparatus available the tablets is kept on an anvil and the force is transmitted by a moving plunger. Many types of hardness testers are available like Stokes or Monsanto, Strong-Cobb, Pfizer, Erweka, and Schleuinger.

**Friability:** It also called the test for abrasion or the mechanical robustness. Roche friabilator is one of the most common devices used to test for resistant to abrasion. In these test 6-20 tablets are placed in a 12 inch high drum

which is rotated for 100 revolutions. A shaped arm lifts and drops the tablets at half the height of the drum. At the end of the operation the tablets are removed deducted and reweighted.

The value is expressed as a percentage. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. Normally, when capping occurs, friability values are not calculated. A thick tablet may have less tendency to cap whereas thin tablets of large diameter often show extensive capping, thus indicating that tablets with greater thickness have reduced internal stress. [10]

**Size and shape**

The shape and dimensions of compressed tablets are determined by the type of tooling during the compression process. At a constant compressive load, tablets thickness varies with changes in die fill, particle size distribution and packing of the powder mix being compressed and with tablet weight, while with a constant die fill, thickness varies with variation in compressive load. Tablet thickness is consistent from batch to batch or within a batch only if the tablet granulation or powder blend is adequately consistent in particle size and particle size distribution, if the punch tooling is of consistent length, and if the tablet press is clean and in good working condition. The thickness of individual tablets may be measured with a micrometer, which permits accurate measurements and provides information of the variation between tablets. Tablet thickness should be controlled within a ±5% variation of a standard value. Any variation in thickness within a particular lot of tablets or between manufacturer's lots should not be apparent to the unaided eye for consumer acceptance of the product. In addition, thickness must be controlled to facilitate packaging.[11]

**Disintegration**

Place the apparatuses in a vessel of suitable diameter containing water at $36^{o}$ to $37^{o}$.adjust the level of the liquid by the gradual addition of water at $36^{o}$ to$37^{o}$ to until the perforations in the metal disc are just converted by a uniform layer of water. Place one vaginal tablet on the upper perforated disc and cover the apparatus with a glass plate to maintain appropriate conditions of humidity. [12]

**Bioadhesive strength of tablets**

The Bioadhesive measurement was performed by using a modified balance method intact with mucosal membrane of goat vagina in vitro as reported by Sanjay garg et al for tablet Bioadhesive measurement. The two pan of physical balance were removed. Right side pan was replaced with a 100ml beaker(A), and on left side glass slide was handed on which vaginal membrane was attached .For balancing the assembly a weight was hangs on left side. A glass container placed left side. A glass block (B) was kept inside the glass container. Above this glass block, a glass slide was placed on which vaginal membrane also attached. The height of this set up was adjusted to leaving a space of about 0.2 cm between two vaginal membrane faces. The set up was balanced by hanging 20gm. Weight on left side. The tablet was placed between two vaginal membrane forces, little pressure to form bioadhesion band, then slowly drop of water added on right side beaker, till the film separated from one side vaginal membrane. Convert volume of water added, to mass. This gave the Bioadhesive strength of tablets in gm.[13]

**Swelling behaviour of bio adhesive tablets**

The extent of swelling was measured in terms of percentage weight gain by the tablets. The swelling behaviour of all the formulations was studied. One tablet from each formulation was kept in Petri dish containing. Acetate buffer $P^H$ 4.7. At the end of 0.5, 1, 2,4hrs tablets were withdrawn, soaked on tissue paper and weighed, and then percentage weight gain by the tablet. With the help of below giving formula calculated the swelling index.[14]

Swelling Index = Final weight - Initial weight / Initial weight x 100

**In-vitro drug release study of bioadhesive vaginal tablets**

In-vitro drug release studies were carried using USP type II dissolution apparatus (paddle type) at 50 rpm. The dissolution medium consisted of 900ml acetate buffer pH 4.7 and dissolution was carried out for 10hr and 24hr maintain the temperature at $37^O$ C. Aliquots of 5ml was withdrawn at one hour for six sample and then 2hr interval and finally 10hr and maintain the sink condition. The aliquots were filtered and the absorbance was measured in each case. Finally the cumulative release percentage of drug release was determined.[15,16]

**Drug release mechanism and kinetics**

In order to established the mechanism and kinetics of drug release form the bioadhesive vaginal tablets ,the experimental data obtained from the in vitro dissolution study was fitted with different kinetic model like zero order (% cumulative release vs. time),first order (log% cumulative amount unabsorbed vs. time), Higuchi's model (%cumulative release vs. √t ) etc. The n value could be characterizing different release mechanism as per the table below.[17,18,19]

**Results and discussion**

Fluconazole loaded bioadhesive vaginal tablets were prepared by direct compression method by using various grades of bioadhesive polymer, such as Carbopol-940, Carbopol-934, HPMC, and Guar gum with other formulation additives. The micromeritic study of powder revealed that the angle of repose of powder ranged from 227.35±1.00 to 264.45±0.27 which indicates good flowability of powder. Bulk density and Tapped density values ranged from 0.38±0.010 to 0.42±0.072 and 0.52±0.007 to 0.56±0.016 respectively. The Haunser's ratio was found between 1.28 to 1.34 and the lower compressibility index. Powder with Carr's index values around 21% and below are considered to have fair and excellent flow properties.The physicochemical study on formulations revealed that the weight variation of all the formulations were within the specified range 4.16±0.16 to 8.66±0.16. The hardness of formulations ranged from 4.16±0.16 to 8.66±0.16.The fastest disintegration occurs in Guar gum 2.2hr. Where else the prolonged disintegration is of 7hr. in pH 4.7. Form Tab.3 since all the formulations are within the acceptable friability range (0.8 to 1%) thus the polymer can be used in the formulation of tablets. Diameter and thickness range was found 6.23 and 5.22. Bioadhesive vaginal tablets formulation in goat vagina and the result showed that all vaginal bioadhesive strengths were found in the range of 5gm. to 13gm.Carbopol was showed better bioadhesive strength. Swelling index lied in the range 0.043 to0.712.The highest swelling was achieved by carbopol bioadhesive vaginal tablets formulation. The swelling index was varied in the various polymer concentrations. The constant drug release form all the Bioadhesive tablet formulation was observed over 10 hr. The in vitro drug release profile of 16 formulations ranged from 19-50% after 10 hours in acetate buffer pH 4.7 The release mechanism was

influenced by the different bioadhesive polymer.BVT-1,BVT-3,BVT-5,BVT-6,BVT-7,BVT-11,BVT-12,BVT-13,BVT-15,BVT-16 which was followed the non Fickian (n>0.5) diffusion mechanism and BVT-2,BVT-4,BVT-8,BVT-9,BVT-10and BVT-14 follows Fickian (n<0.5) transport mechanism. The in vitro drug release profile of 16 formulations ranged from 19-50% after 10 hours in acetate buffer pH 4.7. From this 7 formulations were further studied for 24 hours in acetate buffer pH 4.7 based on the slowest release pattern. From 24$^{th}$ hr release, the drug release kinetic was studied and most of the formulations follow Higuchisquare Root (BVT-1, BVT-3, BVT-5, BVT-7, BVT-11, BVT-12, BVT-16,). Bioadhesive tablet formulation (BVT-1, BVT-3, BVT-5, BVT-7, BVT-11), follows Anomalous transport (Nondiffusional release), Case I anomalous transport follows BVT-12 and. Diffusing predominantly follows the formulation BVT-16. Diffusion predominantly follows the formulation BVT-4. Accordingly to determine the drug release again, studies were carried out with 7 formulations for optimization of drug formulation.

The vaginal route has been traditionally used for the local application of drugs, but is now gaining importance as a possible site for systemic delivery. For the prevention of STDs, AIDS, fungal/ bacterial infections and conception, the use of vaginal products might provide a better alternative to behavioral modifications and the use of condoms. Novel developments such as bioadhesive systems and liposomes overcome some of the major limitations of conventional vaginal products. The consideration of women's opinions on vaginal products is also important for the development of acceptable dosage forms and better compliance. Extensive research is required for a reasonable understanding of various aspects of vaginal drug delivery and rational development of user-friendly formulations.

**Tabe.1- Formulation Design of Bioadhesive Vaginal Tablets with various polymers.**

| Ratio | Drug (mg) | Carbopol -940(mg) | Carbopol -934(mg) | HPMC (mg) | Guar gum (mg) | Starch (mg) | Magnesium Stearate (mg) |
|---|---|---|---|---|---|---|---|
| BVT-1(1:0.5) | 100 | 50 | - | - | - | 97.5 | 2.5 |
| BVT-2(1:0.75) | 100 | 75 | - | - | - | 72.5 | 2.5 |
| BVT-3(1:1) | 100 | 100 | - | - | - | 47.5 | 2.5 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| BVT-4(1:1.25) | 100 | 125 | - | - | - | 22.5 | 2.5 |
| BVT-5(1:0.5) | 100 | - | 50 | - | - | 97.5 | 2.5 |
| BVT-6(1:0.75) | 100 | - | 75 | - | - | 72.5 | 2.5 |
| BVT-7(1:1) | 100 | - | 100 | - | - | 47.5 | 2.5 |
| BVT-8(1:1.25) | 100 | - | 125 | - | - | 22.5 | 2.5 |
| BVT-9(1:0.5) | 100 | - | - | 50 | - | 97.5 | 2.5 |
| BVT-10(1:0.75) | 100 | - | - | 75 | - | 72.5 | 2.5 |
| BVT-11(1:1) | 100 | - | - | 100 | - | 47.5 | 2.5 |
| BVT-12(1:1.25) | 100 | - | - | 125 | - | 22.5 | 2.5 |
| BVT-13(1:0.5) | 100 | - | - | - | 50 | 97.5 | 2.5 |
| BVT-14(1:0.75) | 100 | - | - | - | 75 | 72.5 | 2.5 |
| BVT-15(1:1) | 100 | - | - | - | 100 | 47.5 | 2.5 |
| BVT-16(1:1.25) | 100 | - | - | - | 125 | 22.5 | 2.5 |

**Table.2- Angle of Repose, Bulk density and Tapped density of drug and additives**

| Formulation | Angle of Repose(θ) mean±S.D | Bulk density(Pb) mean±S.D | Tapped density(pt) mean±S.D |
|---|---|---|---|
| **Carbopol-940** | | | |
| 1:0.5(BVT-1) | 21.13±1.57 | 0.42±0.008 | 0.56±0.017 |
| 1:0.75(BVT-2) | 24.22±0.95 | 0.40±0.042 | 0.52±0.022 |
| 1:1(BVT-3) | 19.11±0.67 | 0.38±0.010 | 0.50±0.014 |
| 1:1.25(BVT-4) | 20.22±0.12 | 0.39±0.005 | 0.53±0.017 |
| **Carbopol-934** | | | |
| 1:0.5(BVT-5) | 21.76±0.22 | 0.41±0.007 | 0.53±0.012 |
| 1:0.75(BVT-6) | 22.05±0.58 | 0.42±0.072 | 0.56±0.014 |
| 1:1(BVT-7) | 24.21±0.47 | 0.40±0.007 | 0.52±0.007 |
| 1:1.25(BVT-8) | 22.12±0.16 | 0.41±0.010 | 0.55±0.015 |
| **H.P.M.C** | | | |
| 1:0.5(BVT-9) | 20.22±0.69 | 0.38±0.085 | 0.50±0.014 |
| 1:0.75(BVT-10) | 22.44±0.70 | 0.40±0.010 | 0.53±0.014 |
| 1:1(BVT-11) | 20.33±0.52 | 0.42±0.011 | 0.56±0.016 |
| 1:1.25(BVT-12) | 21.13±0.73 | 0.40±0.089 | 0.53±0.012 |
| **Guar gum** | | | |
| 1:0.5(BVT-13) | 20.14±1.53 | 0.42±0.010 | 0.58±0.019 |
| 1:0.75(BVT-14) | 23.06±0.25 | 0.41±0.014 | 0.53±0.014 |
| 1:1(BVT-15) | 21.12±1.37 | 0.41±0.010 | 0.56±0.020 |
| 1:1.25(BVT-16) | 22.34±1.43 | 0.41±0.012 | 0.56±0.011 |

**Table.3 - Hausner'sratio, Compressibility index Bulk of drug and additives**

| Formulation | Hausner's ratio mean±S.D | Compressibility index(%) mean±S.D |
|---|---|---|
| **Carbopol-940** | | |
| 1:0.5(BVT-1) | 1.35±0.009 | 26.03±0.045 |
| 1:0.75(BVT-2) | 1.30±0.042 | 24.06±0.046 |
| 1:1(BVT-3) | 1.32±0.009 | 26.53±0.046 |
| 1:1.25(BVT-4) | 1.34±0.026 | 25.60±0.276 |
| **Carbopol-934** | | |
| 1:0.5(BVT-5) | 1.30±0.014 | 23.53±0.860 |
| 1:0.75(BVT-6) | 1.33±0.005 | 26.00±1.070 |
| 1:1(BVT-7) | 1.28±0.070 | 23.96±0.230 |
| 1:1.25(BVT-8) | 1.32±0.010 | 25.60±0.630 |
| **H.P.M.C** | | |
| 1:0.5(BVT-9) | 1.30±0.017 | 24.90±0.970 |
| 1:0.75(BVT-10) | 1.30±0.040 | 24.40±1.052 |
| 1:1(BVT-11) | 1.33±0.014 | 25.80±1.000 |
| 1:1.25(BVT-12) | 1.32±0.020 | 25.70±1.380 |
| **Guar gum** | | |
| 1:0.5(BVT-13) | 1.35±0.009 | 27.20±1.350 |
| 1:0.75(BVT-14) | 1.30±0.034 | 22.90±1.052 |
| 1:1(BVT-15) | 1.34±0.012 | 26.50±0.030 |
| 1:1.25(BVT-16) | 1.34±0.080 | 26.36±0.380 |

**Table.4 - Weight Variation, Hardness and Disintegration Time in various formulations.**

| Formulation | Weight Variation (mg) mean±S.D | Hardness ($kg/cm^2$) mean±S.D | Disintegration Hr |
|---|---|---|---|
| **Carbopol-940** | | | |
| 1:0.5(BVT-1) | 231.30±0.41 | 7.33±0.32 | 3 |
| 1:0.75(BVT-2) | 241.40±0.65 | 8.66±0.16 | 3.5 |
| 1:1(BVT-3) | 227.35±1.00 | 8.33±0.33 | 4 |
| 1:1.25(BVT-4) | 230.55±1.31 | 7.33±0.33 | 4 |
| **Carbopol-934** | | | |
| 1:0.5(BVT-5) | 248.50±0.46 | 4.60±0.170 | 6 |
| 1:0.75(BVT-6) | 246.95±0.35 | 5.10±0.170 | 7 |
| 1:1(BVT-7) | 249.15±0.04 | 5.60±0.180 | 7.5 |
| 1:1.25(BVT-8) | 252.55±0.95 | 6.50±0.300 | 7 |

| | | | |
|---|---|---|---|
| **H.P.M.C** | | | |
| 1:0.5(BVT-9) | 249.75±0.48 | 4.66±0.16 | 4 |
| 1:0.75(BVT-10) | 245.80±0.65 | 4.66±0.37 | 4.3 |
| 1:1(BVT-11) | 250.00±0.52 | 4.16±0.16 | 4.8 |
| 1:1.25(BVT-12) | 249.90±0.77 | 4.16±0.09 | 4.2 |
| **Guar gum** | | | |
| 1:0.5(BVT-13) | 262.55±0.87 | 7.50±0.28 | 2.2 |
| 1:0.75(BVT-14) | 260.60±0.50 | 8.00±0.28 | 2.3 |
| 1:1(BVT-15) | 263.55±0.63 | 8.16±0.44 | 2.4 |
| 1:1.25(BVT-16) | 264.45±0.27 | 5.00±0.11 | 2.2 |

**Table.5- Friability, Diameter, Thickness in various formulations.**

| Formulation | Friability (%) | Diameter (mm) mean±S.D | Thickness (mm) mean±S.D |
|---|---|---|---|
| **Carbopol-940** | | | |
| 1:0.5(BVT-1) | 0.12 | 6.17±0.025 | 5.13±0.059 |
| 1:0.75(BVT-2) | 0.1 | 6.20±0.033 | 5.26±0.017 |
| 1:1(BVT-3) | 0.13 | 6.19±0.029 | 5.23±0.023 |
| 1:1.25(BVT-4) | 0.22 | 6.16±0.014 | 5.25±0.040 |
| **Carbopol-934** | | | |
| 1:0.5(BVT-5) | 0.16 | 6.22±0.01 | 5.50±0.015 |
| 1:0.75(BVT-6) | 0.30 | 6.13±0.02 | 5.33±0.011 |
| 1:1(BVT-7) | 0.06 | 6.27±0.07 | 5.19±0.020 |
| 1:1.25(BVT-8) | 0.15 | 6.23±0.01 | 5.23±0.110 |
| **H.P.M.C** | | | |
| 1:0.5(BVT-9) | 0.04 | 6.23±0.015 | 5.33±0.010 |
| 1:0.75(BVT-10) | 0.24 | 6.14±0.014 | 5.34±0.011 |
| 1:1(BVT-11) | 0.02 | 6.38±0.008 | 5.22±0.017 |
| 1:1.25(BVT-12) | 0.18 | 6.29±0.044 | 5.34±0.010 |
| **Guar gum** | | | |
| 1:0.5(BVT-13) | 0.17 | 6.20±0.027 | 5.43±0.013 |
| 1:0.75(BVT-14) | 0.19 | 6.32±0.094 | 5.18±0.050 |
| 1:1(BVT-15) | 0.12 | 6.38±0.031 | 5.44±0.018 |
| 1:1.25(BVT-16) | 0.15 | 6.22±0.017 | 5.43±0.013 |

**Table.6- Bioadhesion strength measurement study of Bioadhesive vaginal tablet formulation.**

| Formulation | Bioadhesive Strength (gm) |
|---|---|
| **Carbopol-940** | |
| 1:0.5(BVT-1) | 13 |
| 1:0.75(BVT-2) | 8 |
| 1:1(BVT-3) | 8 |
| 1:1.25(BVT-4) | 10 |
| **Carbopol-934** | |
| 1:0.5(BVT-5) | 12 |
| 1:0.75(BVT-6) | 9 |
| 1:1(BVT-7) | 13 |
| 1:1.25(BVT-8) | 10 |
| **H.P.M.C** | |
| 1:0.5(BVT-9) | 7 |
| 1:0.75(BVT-10) | 9 |
| 1:1(BVT-11) | 8 |
| 1:1.25(BVT-12) | 10 |
| **Guar gum** | |
| 1:0.5(BVT-13) | 7 |
| 1:0.75(BVT-14) | 6 |
| 1:1(BVT-15) | 5 |
| 1:1.25(BVT-16) | 8 |

**Table.7- Swelling Index measurement study of Bioadhesive vaginal tablet formulation in Acetate buffer $P^H$ 4.7**

| Formulation | Swelling Index (hr) | | | |
|---|---|---|---|---|
| | 0.5 | 1 | 2 | 4 |
| **Carbopol-940** | | | | |
| 1:0.5(BVT-1) | 0.192 | 0.210 | 0.387 | 0.540 |
| 1:0.75(BVT-2) | 0.243 | 0.343 | 0.421 | 0.632 |
| 1:1(BVT-3) | 0.216 | 0.354 | 0.423 | 0.523 |
| 1:1.25(BVT-4) | 0.198 | 0.312 | 0.413 | 0.550 |
| **Carbopol-934** | | | | |
| 1:0.5(BVT-5) | 0.092 | 0.113 | 0.487 | 0.712 |
| 1:0.75(BVT-6) | 0.043 | 0.240 | 0.326 | 0.689 |
| 1:1(BVT-7) | 0.116 | 0.214 | 0.443 | 0.690 |
| 1:1.25(BVT-8) | 0.098 | 0.112 | 0.316 | 0.650 |
| **H.P.M.C** | | | | |
| 1:0.5(BVT-9) | 0.245 | 0.310 | 0.487 | 0.503 |
| 1:0.75(BVT-10) | 0.233 | 0.343 | 0.421 | 0.532 |
| 1:1(BVT-11) | 0.216 | 0.344 | 0.398 | 0.623 |
| 1:1.25(BVT-12) | 0.198 | 0.202 | 0.419 | 0.542 |

| | | | | |
|---|---|---|---|---|
| **Guar gum** | | | | |
| 1:0.5(BVT-13) | 0.923 | 1.210 | - | - |
| 1:0.75(BVT-14) | 0.845 | 1.243 | - | - |
| 1:1(BVT-15) | 0.790 | 1.354 | - | - |
| 1:1.25(BVT-16) | 0.898 | 1.312 | - | - |

**Table.8- Release mechanism**

| **"n"value** | **Release Mechanism** |
|---|---|
| **n<0.4** | Case I anomalous transport |
| **0.4<n<0.5** | Diffusion predominantly |
| **n=0.5** | Fickian Diffusion (Higuchi matrix) |
| **0.5<n>1** | Anomalous transport (Nondiffusional release) |
| **n =1** | ClassII transport (Ideal zero order release) |
| **n >1** | Super class II transport |

**Table.9- In-vitro drug release kinetic studies of Bioadhesive vaginal tablet formulation**

| | **Release Profile** | | | | | |
|---|---|---|---|---|---|---|
| **Formulation Code** | **Zero Order Release** | **First Order Release** | **Higuchi square root equation** | **Korsmeyer and Pappas** | | |
| | | **$r^2$** | | **$r^2$** | **N** | **Comment** |
| BVT-1 | 0.954 | 0.903 | 0.973 | 0.820 | 0.788 | Non Fickian |
| BVT-2 | 0.815 | 0.921 | 0.889 | 0.235 | 0.246 | Fickian |
| BVT-3 | 0.973 | 0.919 | 0.978 | 0.800 | 0.703 | Non Fickian |
| BVT-4 | 0.856 | 0.819 | 0.961 | 0.481 | 0.485 | Fickian |
| BVT-5 | 0.973 | 0.929 | 0.989 | 0.841 | 0.681 | Non Fickian |
| BVT-6 | 0.871 | 0.835 | 0.970 | 0.546 | 0.520 | Non Fickian |
| BVT-7 | 0.925 | 0.969 | 0.995 | 0.785 | 0.585 | Non Fickian |
| BVT-8 | 0.633 | 0.662 | 0.804 | 0.296 | 0.326 | Fickian |
| BVT-9 | 0.669 | 0.789 | 0.809 | 0.207 | 0.269 | Fickian |
| BVT-10 | 0.812 | 0.886 | 0.919 | 0.252 | 0.275 | Fickian |
| BVT-11 | 0.912 | 0.840 | 0.954 | 0.884 | 0.941 | Non Fickian |
| BVT-12 | 0.930 | 0.890 | 0.983 | 0.844 | 0.965 | Non Fickian |
| BVT-13 | 0.722 | 0.898 | 0.813 | 0.232 | 0.235 | Fickian |
| BVT-14 | 0.769 | 0.877 | 0.882 | 0.202 | 0.294 | Fickian |
| BVT-15 | 0.840 | 0.825 | 0.926 | 0.581 | 0.594 | Non Fickian |
| BVT-16 | 0.940 | 0.937 | 0.987 | 0.516 | 0.516 | Fickian |

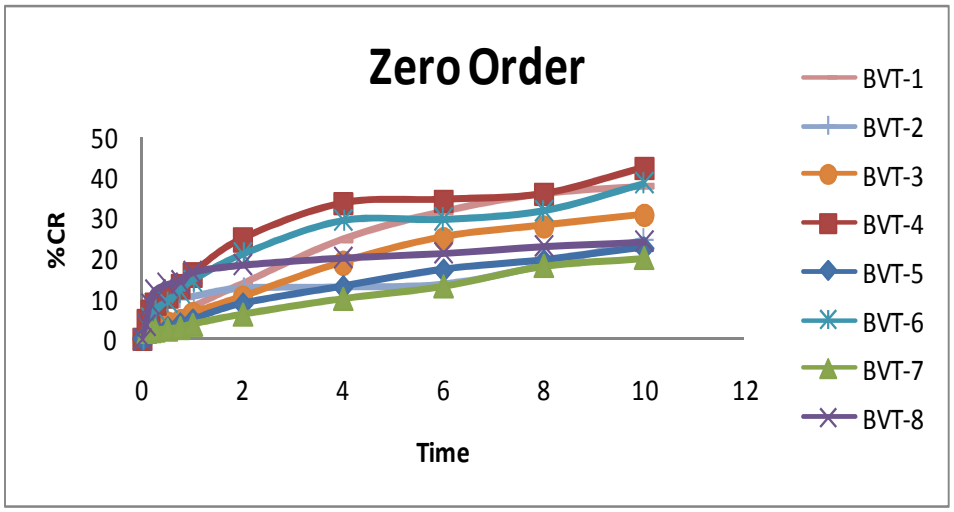


**Fig.1- In-vitro drug release profile of BVT-1 to BVT-8**

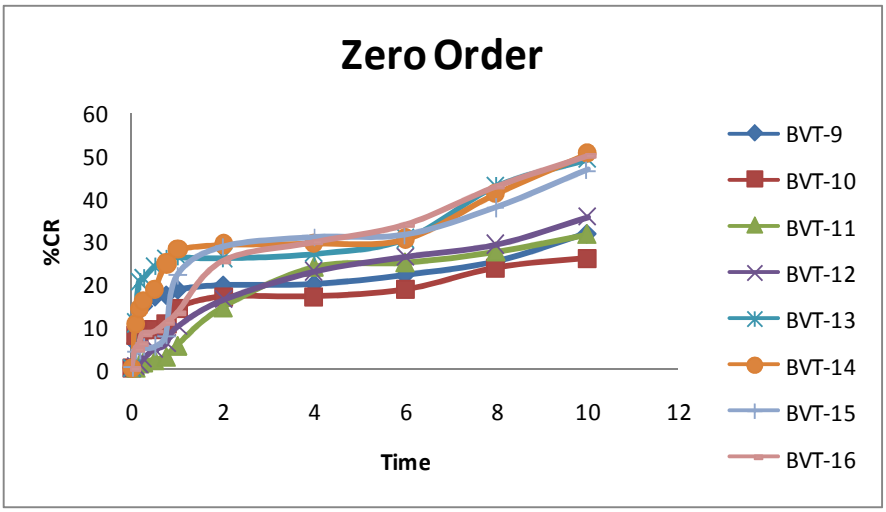


**Fig.2- In-vitro drug release profile of BVT-9 to BVT-16**

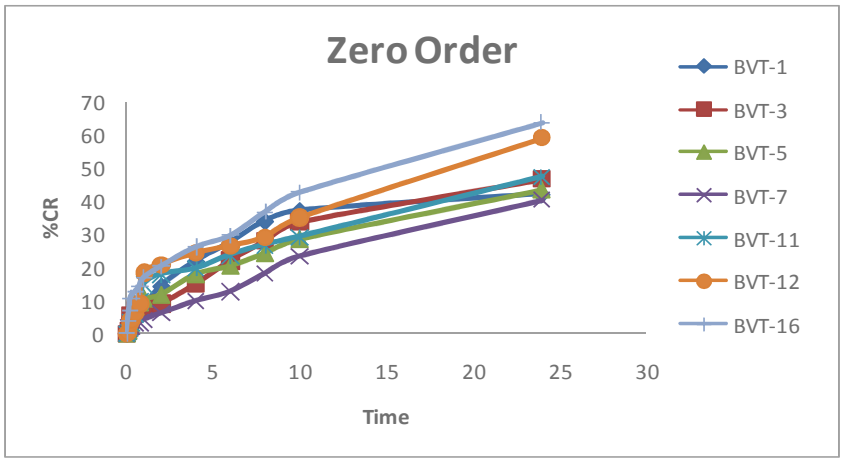


**Fig.3- Zero order release for seven formulation.**

**References**


1. Vermani K and S Garg. The scope and potential of vaginal drug delivery. PSTT 2000;3(10):359-364
2. Deshpande AA. Intravaginal drug delivery. Drug Delivery.1992;18:1225–1279
3. Burgos MH and Linaires CER. Ultrastructure of the vaginal mucosa. In Human Reproductive Medicine: the Human Vagina (Hafez ESE and Evans TN), 1978, North Holland Publishing Company. pp.63–93
4. Benziger DP and Edelson J. Absorption from the vagina. Drug Metab. Rev. 1983;14: 137–168
5. Threpathi KD, Antifungal drugs, "Essential of medical Pharmacology", 5th edition, Year 2004, Jypee Publishers, p. 715-717.
6. Rabia B, Muhammad HS, Noushcen A, Durriya H. Formulation development of Ibuprofen tablets by direct compression method .Pharma.Sci.2008;21(2):113-120.
7. Augsburger LL and Zelhofer JM. Tablets Formulation, In; Encyclopedia of Pharmaceutical Technology Vol.6, James Swarbick, Informa Healthcare USA. Inc 270 Madision Avenue New York 10016;36-41
8. Chaudhari PD, Chudhari SP. Formulation and Evaluation of fast dissolving tablets Famotidin. Indian drug 2005; 42(10), 641-649.
9. Rudnic E and Schwartz J B. Oral solid dosage forms In: Remington's Pharmaceutical Sciences. 18th Ed. 1990. Ed. Gennaro, A. R. Mack Publishing Company. Easton, Pennsylvania, USA. 1633-1665.
10. Banmer GS and AndersonNR. Tablets, In; Lachman L.,Lieberman A.H.,Kanig J.L The Theory and Practical Pharmacy.3rd ed. 2005. Varghese Publishing House Mumbai 400014:293-319.
11. Kattk KM ,Rudward ME. Tablets,In;Modern Pharmaceutics 4th ed. Banker SG, Rhodes TC, Marcel Dekker Inc.270. Modison Avenue New York 10016;43-47
12. British Pharmacopia, Disintegration test for Suppositories and pessaries, international Edt. Landon HMSO. Vol.II.1993. pp.A159-A160.
13. Parodi B, Russo E, Caviglioli G, Cafaggi S, Bignardi G. Development and characterization of a buccoadhesive dosage form of oxycodone hydrochloride. Drug Delevery. Ind. Pharm 1996; 22:445-450.

14. Dandagi PM, Mastihomath VS, Patil MB, Manvir FV, Gadad AP. Development and Evaluation of Theophyllin and Salbutamal Sulphate Sustain Release matrix tablets,Ind.j.Pharm. Sci 2005;67(5):598-602.
15. British Pharmacopia,Dissolution Test for Tablets and Capsules, international Edt.Landon HMSO. vol.II.(1993)pp.A159-A160.
16. Kamel EL. Chitosen and sodium alginate-Based Bioadhesive Vaginal Tablets. AAPS Pharm.Science 2002;4(4):1-7.
17. Nicolas C, Marc G, Gaelle R, Dominique C. Studies of release kinetics of small and high molecular weight sustained dispersed into spray dried ethylcellulose microspheres, J Control Release 2002;84:125-135.
18. Morkhade DM, Fulzele SV, Satturwar PM, Joshi SB. Gum copal and gum dammer: novel matrix forming material for sustain release drug delivery. Ind j Pharm.sci 2006;68(1):53-58.
19. Higuchi T. Mechanism of rate of sustained action medication. J Pharm. Sci 1963; 52(11):1145-1149.

**"*Corresponding author"**

**Rohit Bisht***
Assistant Professor
Siddartha Institute of Pharmacy
Do bachi, Near I.T-Park
Sahastradhara road, Dehradun
Uttarakhand-248001
Email: rohit_thakur1234@rediffmail.com