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Research Article

**FORMULATION AND EVALUATION OF RISPERIDONE
MUCOADHESIVE BUCCAL TABLETS**Praveen Gujjula¹, S. K Godasu², D. Varun³, Nimma.vijayarekha⁴, G. Anusha⁵^{1,2} Associate professor, Sri Indu Institute of Pharmacy^{4,5} Assistant professor, Sri Indu Institute of Pharmacy³ Professor & Principal, Sri Indu Institute of Pharmacy**Article Received:** January 2023**Accepted:** January 2023**Published:** February 2023**Abstract:**

In the present work, an attempt was made to design efficacious and prolonged release mucoadhesive buccal tablets of Risperidone using various polymers to reduce dosing frequency, decrease gastric irritation and to improve patient compliance. Two polymer combinations (carbopol 943 and PVP K30 as well as carbopol and xanthan gum) were taken at varying proportions. The buccal tablets were tested for weight uniformity, thickness, friability and hardness. Tablets were then evaluated for their swelling index, in vitro drug release, mucoadhesion time (wash-off time) and ex vivo drug permeation.

The kinetics and mechanism of the drug permeation through the excised buccal tissue of goat from the buccal tablets were also characterized. The data collected were then analyzed using software to determine the effects of each parameter. The effects of the various parameters involved were then interpreted. The best polymer composite was selected from the various ratios of the polymers. The best polymer ratio was found to be Carbopol 934 and PVP K30 in the ratio 1:2. The mucoadhesive strength of buccal tablets increases as the concentration of secondary polymer increases. The above polymer composite had shown satisfactory results in the parameters such as thickness, hardness, drug content, swelling index, mucoadhesive time, in-vitro dissolution and in-vitro diffusion. The satisfactory formulation shows a zero order drug release profile depending on the regression value and shown a satisfactory dissolution profile. Slow, controlled and maximum release of Risperidone over a period of 6 h was obtained from buccal tablets F2 formulation containing Carbopol 934 and PVP K30. 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.

Key words: Formulation, Evaluation, Risperidone, Mucoadhesive Buccal Tablets

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INTRODUCTION

The oral course of medication organization is the most well-known and favored course for drug conveyance, as it empowers simple ingestion, self-prescription, precise dose, adaptable and controlled dosing timetable, and patient consistence with a slim likelihood of organization trouble [1, 2]. It additionally has a few significant detriments, for example, the first-pass impact, gastrointestinal enzymatic corruption, and slow beginning of activity [3]. To defeat these detriments, mucoadhesive medication conveyance and sublingual medication conveyance could be better choices [4].

Mucoadhesive measurement structures are extraordinarily intended to stick to the mucosal surface, in this way escalating maintenance of the medication at the site of use, while giving a controlled pace of medication discharge for better helpful result [5]. To make reference to, a couple of mucoadhesive medication conveyance frameworks are cement patches, glue gels, cement tablets, glue films, cement plates, and so on [6]. A few districts, for example, the gastrointestinal (GI) lot, the urogenital plot, the ear, the nasal course, and the aviation routes in the body are lined by the mucosal layer. These are either single-layered epithelium tracked down in the GI lot, bronchi, and digestion tracts or diverse separated epithelium tracked down in the throat, vagina, and cornea and are the potential destinations where mucoadhesive medication conveyance frameworks can be valuable [6, 7].

Buccal mucosa is one of such mucosal site which has a serious degree of vascularization and empowers direct channel of blood stream into the jugular vein, which assists with keeping away from the conceivable digestion of medications by the gastrointestinal course and liver [8]. The buccal conveyance consequently infers the assimilation of medicine through the

mucosal covering of the buccal pit. More straightforward medication organization, the chance of brief end in the state of unpredicted secondary effects and crises, the chance of consolidating protein inhibitor/penetration enhancer, and so forth are other significant benefits of this medication conveyance framework [9, 10].

Different mucoadhesive polymers (regular, semi-manufactured, and engineered) utilized in this conveyance framework become glue on hydration [11], hence can be utilized for focusing on a medication to a specific district of the body. At first, when the mucoadhesive item is in touch with the mucosal film, it expands and spreads, instating profound contact with the mucosal layer and afterward mucoadhesive materials (polymers) are actuated by the presence of dampness and medication delivers gradually [12].

Risperidone is a second-generation antipsychotic (SGA) medication used in the treatment of a number of mood and mental health conditions including schizophrenia and bipolar disorder. It is one of the most widely used SGAs. Paliperidone, another commonly used SGA, is the primary active metabolite of risperidone (i.e. 9-hydroxyrisperidone). Schizophrenia and various mood disorders are thought to be caused by an excess of dopaminergic D2 and serotonergic 5-HT_{2A} activity, resulting in overactivity of central mesolimbic pathways and mesocortical pathways, respectively. Risperidone is thought to reduce this overactivity through inhibition of dopaminergic D2 receptors and serotonergic 5-HT_{2A} receptors in the brain.

Risperidone binds with a very high affinity to 5-HT_{2A} receptors, approximately 10-20 fold greater than the drug's binding affinity to D2 receptors, and carries lesser activity at several off-targets which may be responsible for some of its undesirable effects. The aim of the present investigation was to formulate Risperidone buccal tablets.

MATERIALS AND METHODS:**Table 1: Materials**

| Sl. no. | Materials | Manufacturer | Application |
|---------|------------------------|---|-----------------------|
| 1. | Risperidone IP | Navakar Biochemical, Gujarat | API |
| 2. | Carbopol grade 934p | Loba Chemicals Private Limited, Hyderabad | Buccoadhesive polymer |
| 3. | PVP K30 | Merck Limited, Mumbai | Buccoadhesive polymer |
| 4. | Xanthan gum | Fisher Scientific, Mumbai | Buccoadhesive polymer |
| 5. | Sodium lauryl sulphate | Loba Chemicals Private limited, Hyderabad | Penetration enhancer |
| 6. | Magnesium stearate | Merck Limited, Mumbai | Lubricant |
| 7. | Talc | Loba Chemicals Private Limited, Hyderabad | Glidant |

Methodology**Pre-compressional Studies****Calibration curve****Preparation of stock solution**

Standard stock solution of Risperidone was prepared by dissolving accurately weighed 10 mg of drug in phosphate buffer pH 6.8 in 100ml volumetric flask to give concentration of 100 µg/ml.

Preparation of standard dilutions

Five 50 ml volumetric flasks were taken. Aliquots of 1 ml, 2ml, 4ml, 6 ml and 8 ml were taken from stock solution and were diluted, made up to the mark to obtain the concentrations as 2 µg/ml, 4 µg/ml, 8 µg/ml, 12 µg/ml and 16 µg/ml respectively. Then it was subjected to UV visible spectrometer at 322 nm. Readings were noted and graph was plotted as shown in fig.16.

Drug polymer compatibility study

To investigate any possible interactions between the drug and the used bioadhesive polymers, infrared spectroscopy was adopted. The IR spectrum of pure drug, polymer as well as physical mixture of drug and polymer was taken, interpreted and compared with each other. The IR spectra was carried out using

Shimadzu IR-470 spectrophotometer. The samples were prepared as potassium bromide discs compressed under a pressure of 6 tons. The scanning range was over 4000-400 cm⁻¹

Formulation of mucoadhesive buccal tablets

Risperidone mucoadhesive tablets were prepared by direct compression method as per the formulations as shown in Table 1. Before direct compression, all the ingredients were sifted through sieve No. 40 and then thoroughly blended in glass mortar and pestle. Blending was carried out separately for core tablet (polymer and drug) and backing layer (ethyl cellulose). The mixture of core tablet was lubricated with magnesium stearate and talc which was already passed through sieve 60.

At first, the core tablets were compressed by using compression machine with 8 mm punch. Then, one compressed core tablet was placed in die cavity manually. Over it, accurately weighed 50 mg of ethyl cellulose was added to each die cavity. It was then leveled and compressed again to obtain Risperidone buccal tablets having one sided backing layer of ethyl cellulose. After compression, the tablets were weighed to check that it lies within the range of 100±10 mg.

Table 2. Formulations prepared by direct compression method

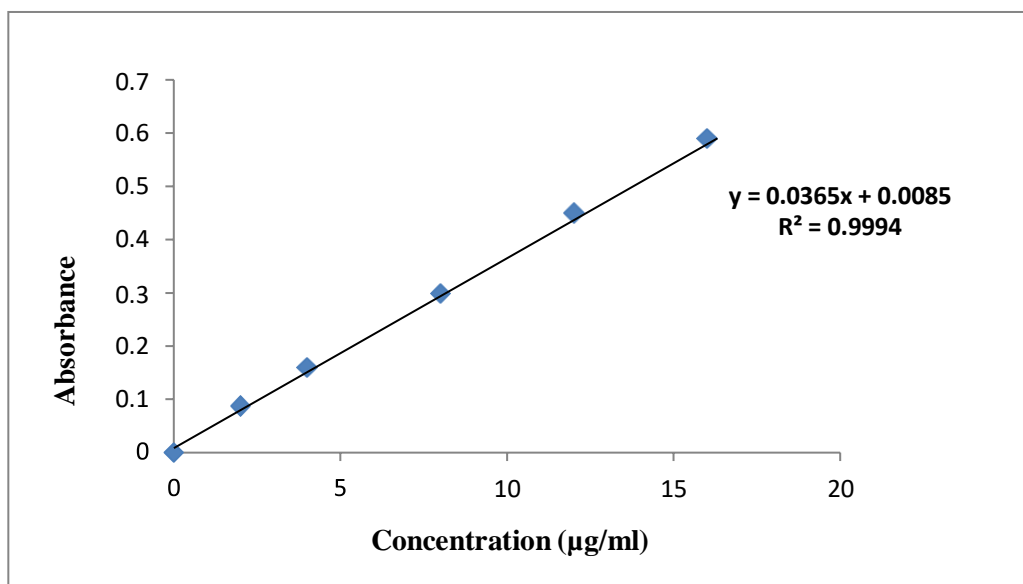
| Formulation code | F1 | F2 | F3 | F4 | F5 | F6 |
|-----------------------------|----|----|------|----|----|------|
| Core tablet | | | | | | |
| Drug(mg) | 10 | 10 | 10 | 10 | 10 | 10 |
| Carbopol 934 (mg) | 18 | 12 | 14.5 | 18 | 12 | 14.5 |
| PVP K30 (mg) | 18 | 24 | 21.5 | - | - | - |
| Xanthan gum (mg) | - | - | - | 18 | 24 | 21.5 |
| Sodium lauryl sulphate (mg) | 2 | 2 | 2 | 2 | 2 | 2 |
| Mg stearate (mg) | 1 | 1 | 1 | 1 | 1 | 1 |
| Talc (mg) | 1 | 1 | 1 | 1 | 1 | 1 |
| Backing Layer | | | | | | |
| Ethyl Cellulose (mg) | 50 | 50 | 50 | 50 | 50 | 50 |

RESULT AND DISCUSSION:**Results****Pre-compressional Evaluations****Calibration curve**

The calibration curve of drug obeyed Beer Lambert's law in the concentration range of 0-16 μ g/ml ($R^2 = 0.9994$) at 322nm and the result is shown in table 4 and plot is shown in fig. 1.

Table 3. Calibration curve of Risperidone in pH 6.8

| Sl. No. | Concentration(μ g/ml) | Absorbance at322 nm |
|---------|----------------------------|---------------------|
| 1 | 2 | 0.087 |
| 2 | 4 | 0.16 |
| 3 | 8 | 0.299 |
| 4 | 10 | 0.45 |
| 5 | 12 | 0.591 |

**Fig. 1. Standard calibration curve of Risperidone in Phosphate buffer pH 6.8**

Compatibility study by FTIR

Fig. 2 presents the results obtained from FT-IR spectroscopy analysis. The spectrum of Risperidone shows characteristic peaks of C-H stretching band at $3,058\text{ cm}^{-1}$, strong C=O stretching band at $1,644\text{ cm}^{-1}$, strong N-O stretching band at $1,533\text{ cm}^{-1}$, C-N stretching of the oxazole ring at $1,350\text{ cm}^{-1}$, strong C-F stretching at $1,130\text{ cm}^{-1}$, and weak C-N stretch of tertiary amine at piperidine ring at $1,192\text{ cm}^{-1}$. The spectrum of PVP K30 gives broad -OH stretching of carboxylic acid at $3,400\text{--}2,800\text{ cm}^{-1}$, C=O stretching of carbonyl group at $1,699\text{ cm}^{-1}$, and C-OH asymmetric stretching band at $1,166\text{ cm}^{-1}$. The spectrum of xanthan gum displays distinct peaks of -OH stretching centered around $3,200\text{ cm}^{-1}$, asymmetric and symmetric -COO- stretching at $1,613\text{ cm}^{-1}$ and $1,417\text{ cm}^{-1}$, respectively, and C-O stretching at $1,025\text{ cm}^{-1}$. All the peaks corresponding to the respective bonds are shown in table 5.

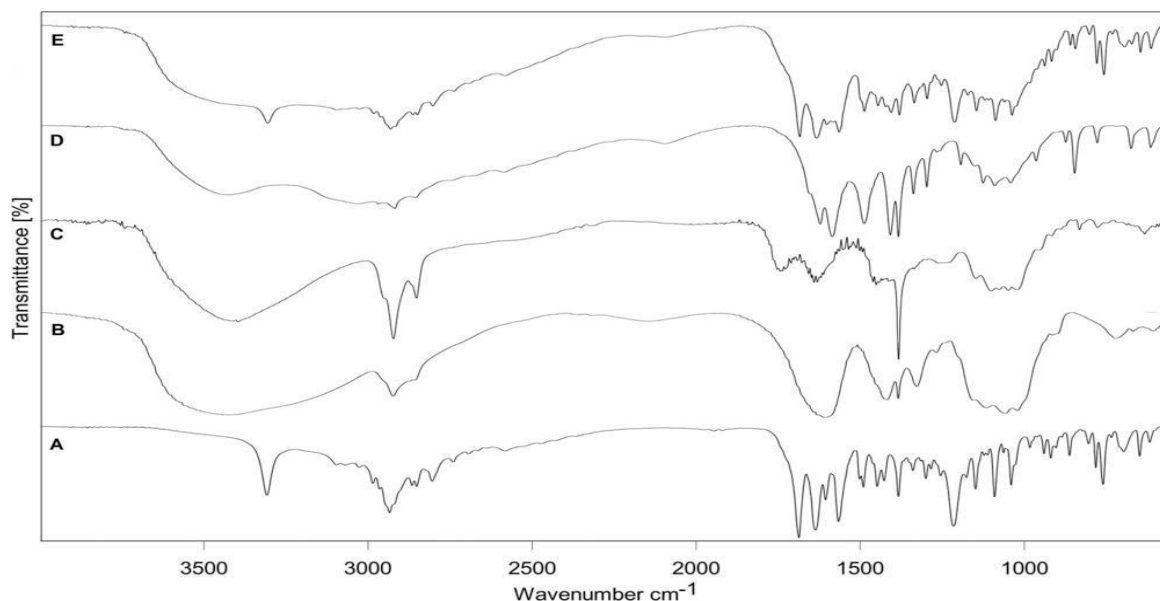


Fig. 2. FTIR spectra of (A)-Risperidone; (B)- PVP K30; (C)- Xanthan gum; (D)- physical mixture of Risperidone, carbopol and PVP 30; (E)- physical mixture of Risperidone, carbopol and xanthan gum

Table 4. Peaks obtained for various chemical bonds.

| Characteristic functional group | Peaks |
|---------------------------------|------------------------|
| -OH stretching | $3,200\text{ cm}^{-1}$ |
| -COO- stretching | $1,417\text{ cm}^{-1}$ |
| -COO- stretching | $1,613\text{ cm}^{-1}$ |
| C-O stretching | $1,025\text{ cm}^{-1}$ |
| C=O stretching | $1,699\text{ cm}^{-1}$ |
| C-F stretching | $1,025\text{ cm}^{-1}$ |
| C-N stretch | $1,192\text{ cm}^{-1}$ |

Risperidone - Buccal Tablet Evaluations

Uniformity of Weight:

The results for the uniformity of weight are tabulated in table 5.

Table 5. Uniformity of Weight

| Sl. No. | Formulation code | Weight uniformity (mg) |
|---------|------------------|------------------------|
| 1. | F1 | 101.3 ± 3.62 |
| 2. | F2 | 99.2 ± 3.32 |
| 3. | F3 | 98.9 ± 1.91 |
| 4. | F4 | 97.3 ± 2.16 |
| 5. | F5 | 102.1 ± 3.02 |
| 6. | F6 | 101.2 ± 2.81 |

Thickness of the Risperidone buccal tablet

The results for the thickness of the Risperidone buccal tablets are tabulated in table 6.

Table 6. Average thickness of the Risperidone buccal tablets

| Sl. No. | Formulationcode | Thickness (mm) |
|---------|-----------------|----------------|
| 1. | F1 | 2.98 ± 0.091 |
| 2. | F2 | 2.60 ± 0.067 |
| 3. | F3 | 2.081 ± 0.08 |
| 4. | F4 | 2.77 ± 0.051 |
| 5. | F5 | 2.75 ± 0.023 |
| 6. | F6 | 2.80 ± 0.053 |

Hardness of the Risperidone buccal tablets

The results for the hardness of the Risperidone buccal tablets are tabulated in Table 7.

Table 7. Average hardness of the Risperidone buccal tablets

| Sl. No. | Formulationcode | Avg.hardness (kg/cm ²) |
|---------|-----------------|------------------------------------|
| 1. | F1 | 3.24 ± 0.23 |
| 2. | F2 | 3.86 ± 0.18 |
| 3. | F3 | 3.63 ± 0.52 |
| 4. | F4 | 4.02 ± 0.09 |
| 5. | F5 | 3.52 ± 0.55 |
| 6. | F6 | 3.90 ± 0.11 |

Friability of the Risperidone buccal tablets

The results for the friability test for the Risperidone buccal tablets are tabulated in table 8.

Table 8. % Friability of the Risperidone buccal tablets

| Sl. No. | Formulation code | Friability (%) |
|---------|------------------|----------------|
| 1. | F1 | 0.164±0.36 |
| 2. | F2 | 0.025±0.21 |
| 3. | F3 | 0.127±0.85 |
| 4. | F4 | 0.478±0.09 |
| 5. | F5 | 0.031±0.11 |
| 6. | F6 | 0.52±0.10 |

Surface pH

The results for the surface pH of the Risperidone buccal tablets are tabulated in table 9.

Table 9. Surface pH of the Risperidone buccal tablets

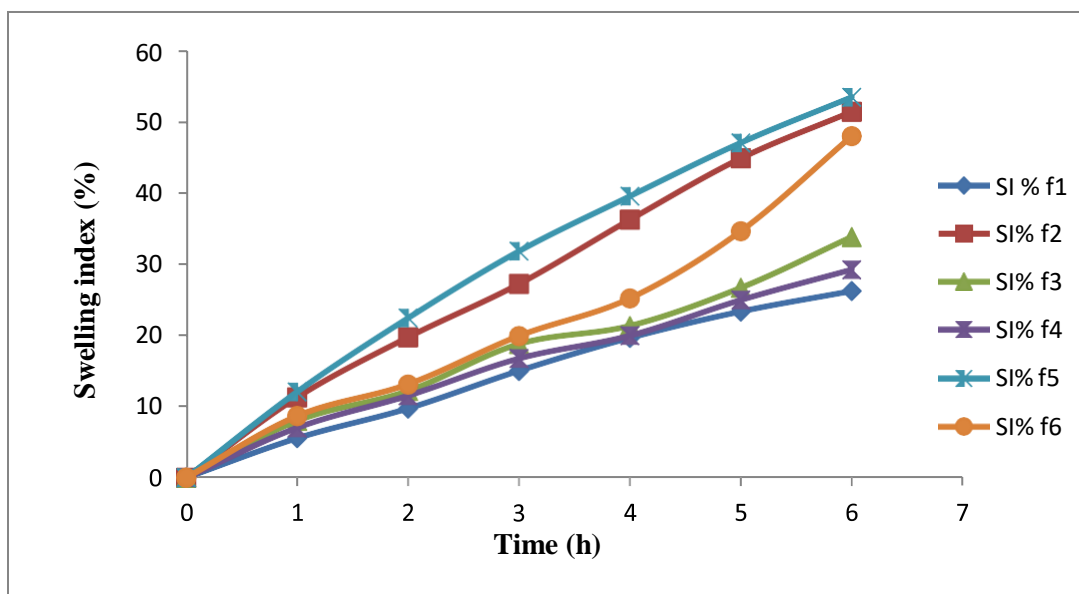
| Sl. No. | Formulation code | Surface pH |
|---------|------------------|-------------|
| 1 | F1 | 6.78 ± 0.05 |
| 2 | F2 | 6.88 ± 0.10 |
| 3 | F3 | 7.01 ± 0.02 |
| 4 | F4 | 6.90 ± 0.05 |
| 5 | F5 | 6.83 ± 0.01 |
| 6 | F6 | 6.99 ± 0.21 |

Swelling Index

The swelling index of the various buccal formulations are tabulated in Table 10. The extent of swelling is represented in Fig. 3.

Table 10. Swelling index (%) of the Risperidone buccal tablets

| Formulation code | Time (h) | | | | | |
|------------------|------------|------------|------------|------------|------------|-------------|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| F1 | 5.55±1.11 | 9.72±0.77 | 15.01±0.67 | 19.63±1.12 | 23.33±0.45 | 26.2±0.31 |
| F2 | 11.28±1.09 | 19.71±0.87 | 27.91±0.99 | 36.21±1.33 | 44.83±0.96 | 51.37±0.14 |
| F3 | 7.99±0.91 | 12.18±0.99 | 18.77±1.12 | 21.31±0.63 | 26.66±1.19 | 33.81±1.23 |
| F4 | 7.01±0.87 | 11.51±0.78 | 16.73±0.99 | 19.94±0.76 | 24.94±0.67 | 29.21±1.121 |
| F5 | 12.06±0.75 | 22.41±1.22 | 31.79±1.11 | 39.51±0.54 | 47.01±0.79 | 53.42±0.51 |
| F6 | 8.67±0.91 | 13.12±2.01 | 19.91±1.23 | 25.18±1.45 | 34.61±0.61 | 47.95±0.66 |

**Fig. 3. Swelling index(%) for all formulations**

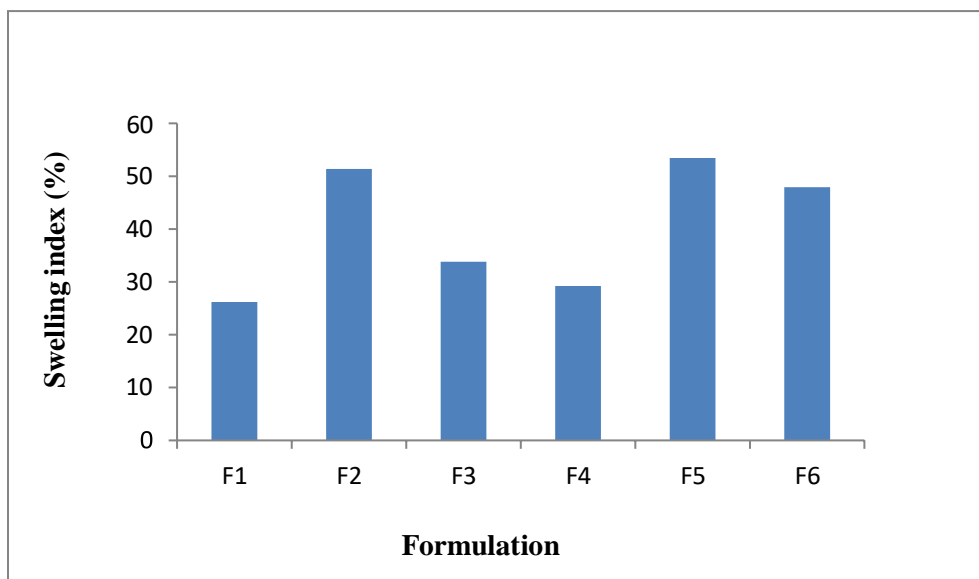


Fig. 4. Extent of swelling in all formulation

Mucoadhesive time (Wash-off test)

The data from the Wash off test are tabulated in table 11.

Table 11. Time duration of attachment of the Risperidone buccal tablets

| Sl. No. | Formulationcode | Mucoadhesivetime |
|---------|-----------------|------------------|
| 1. | F1 | > 6 h |
| 2. | F2 | 5 h 38 min |
| 3. | F3 | 5 h 49 min |
| 4. | F4 | > 6h |
| 5. | F5 | 5 h 31 min |
| 6. | F6 | 5 h 45 min |

In vitro drug release study

The data obtained from the in vitro drug release study are represented in table 12 for formulations F1, F2, F3 and in table 13 for formulation F4, F5, F6.

The in-vitro dissolution profile for the various Risperidone buccal tablet formulations is given below in Fig. 5 for formulation F1, F2, F3 and in Fig. 21 for formulations F4, F5, F6.

Table 12. Cumulative percentage in-vitro drug release of Risperidone buccal tablet formulations F1, F2, F3

| Time (min) | F1 | F2 | F3 |
|------------|------------|------------|------------|
| 15 | 10.11±0.77 | 15.51±0.54 | 11.39±0.66 |
| 45 | 23.32±0.56 | 26.79±0.34 | 21.88±0.15 |
| 60 | 30.62±0.65 | 41.57±1.22 | 36.63±2.02 |
| 120 | 40.01±0.97 | 62.91±1.34 | 55.15±1.01 |
| 180 | 51.23±0.78 | 76.98±0.17 | 67.29±0.81 |
| 240 | 66.61±0.51 | 83.62±0.19 | 70.31±0.14 |
| 300 | 74.41±0.18 | 93.11±0.99 | 74.05±0.22 |
| 360 | 78.32±0.88 | 98.25±0.23 | 83.50±0.12 |

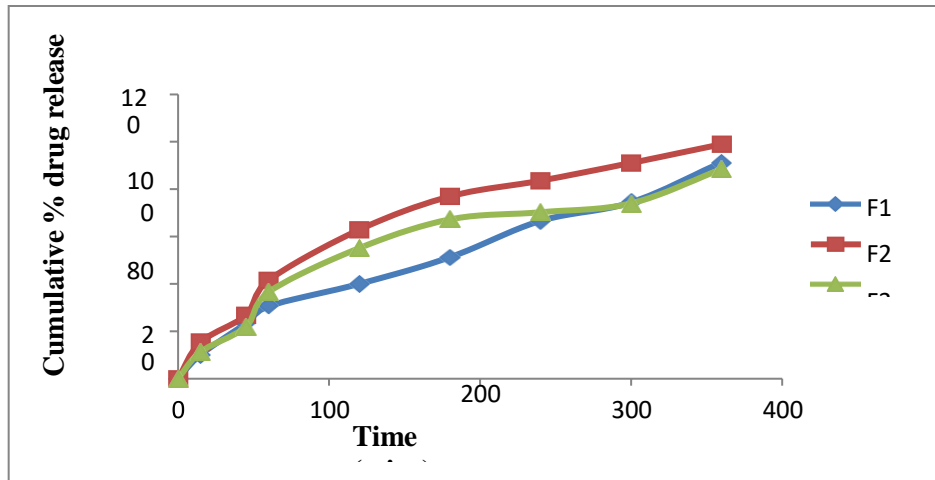


Fig. 5. In vitro dissolution profiles of Risperidone buccal tablet formulations F1 ,F2, F3

Table 13. Cumulative percentage in-vitro drug release of Risperidone buccal tabletformulations F4,F5,F6

| Time (min) | F4 | F5 | F6 |
|------------|------------|------------|------------|
| 15 | 15.77±1.22 | 14.38±1.34 | 12.41±0.79 |
| 45 | 23.12±1.34 | 29.11±1.77 | 25.62±0.56 |
| 60 | 41.23±0.36 | 55.31±0.99 | 46.97±1.11 |
| 120 | 52.79±1.91 | 74.92±2.01 | 61.66±1.04 |
| 180 | 61.44±0.87 | 80.96±1.31 | 75.32±0.67 |
| 240 | 72.52±0.48 | 91.73±0.22 | 77.81±1.22 |
| 300 | 77.92±0.53 | 93.41±1.23 | 81.33±0.33 |
| 360 | 81.34±0.65 | 96.54±0.88 | 87.32±1.04 |

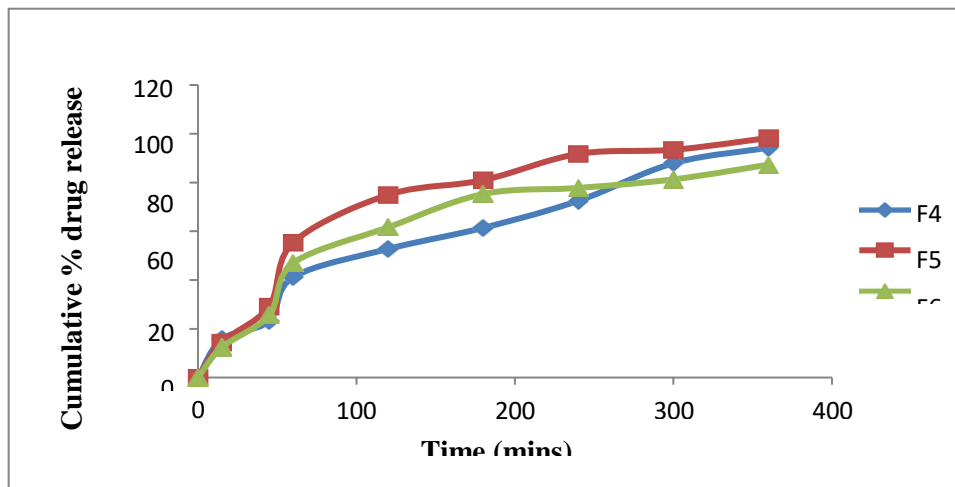


Fig. 6. In vitro dissolution profiles of Risperidone buccal tablet formulations F4, F5, F6

Ex vivo drug permeation study

The drug permeation data for the various Risperidone buccal tablet formulations is given below in table 14 for formulation F1, F2, F3 and in table 16 for formulations F4, F5, F6.

The ex vivo drug permeation profile for the various Risperidone buccal tablet formulations is given below in Fig. 7 for formulation F1, F2, F3 and in Fig. 8 for formulations F4, F5, F6.

Table 14. Cumulative percentage drug permeation for Risperidone buccal tablet formulations F1, F2, F3

| Time (min) | F1 | F2 | F3 |
|------------|------------|-------------|------------|
| 15 | 8.93±1.28 | 11.2±1.22 | 7.32±1.24 |
| 45 | 20.13±1.45 | 25.42±0.56 | 21.01±0.63 |
| 60 | 29.86±1.71 | 31.3±0.34 | 30.51±1.05 |
| 120 | 36.23±2.04 | 49.71±2.01 | 40.13±1.12 |
| 180 | 47.51±2.11 | 66.32±1.73 | 56.91±0.89 |
| 240 | 56.31±0.66 | 79.52±0.77 | 60.91±0.67 |
| 300 | 68.92±0.79 | 83.08±0.225 | 79.70±0.35 |
| 360 | 72.63±0.71 | 96.63±0.23 | 83.55±0.78 |

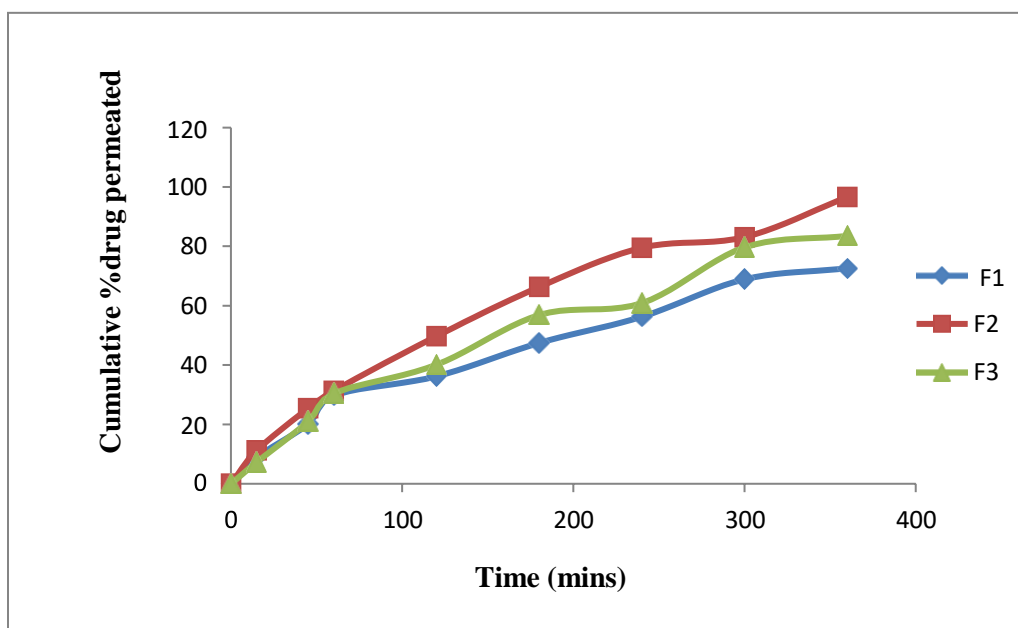
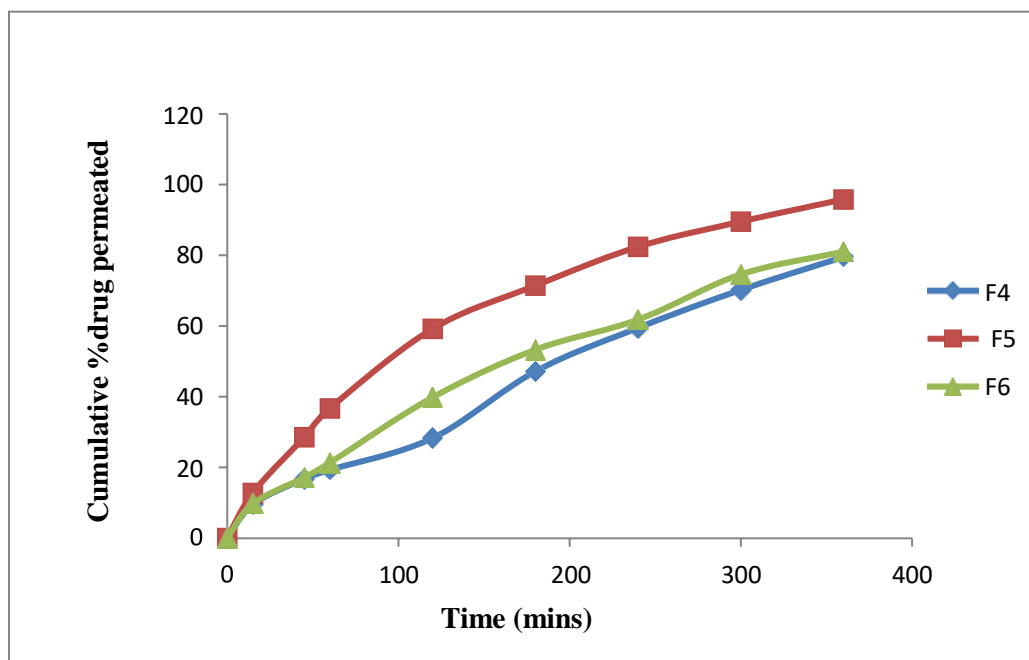


Fig. 7. Ex-vivo diffusion profile of Risperidone buccal tablet formulations F1, F2, F3

Table 15. Cumulative percentage drug permeation for Risperidone buccal tablet formulations F4, F5, F6

| Time (min) | F4 | F5 | F6 |
|------------|------------|------------|------------|
| 15 | 9.58±0.64 | 12.81±1.55 | 9.77±0.89 |
| 45 | 16.8±1.33 | 28.52±1.79 | 17.12±0.78 |
| 60 | 19.35±1.92 | 36.71±0.89 | 21.33±1.76 |
| 120 | 28.3±0.91 | 59.21±0.86 | 39.82±1.54 |
| 180 | 47.17±0.75 | 71.39±0.78 | 53.27±1.03 |
| 240 | 59.5±0.47 | 82.4±1.27 | 61.8±1.07 |
| 300 | 70.23±0.59 | 89.51±1.11 | 74.59±0.74 |
| 360 | 79.54±1.63 | 95.81±0.36 | 81.03±0.97 |

**Fig. 8. Ex-vivo diffusion profile of Risperidone buccal tablet formulations F4, F5, F6**

Drug release kinetics for the buccal tablet formulations

Out of all the prepared formulation, F2 was selected as optimized formulation as it gave the best results for cumulative percentage drug release.

The drug release kinetics for the optimized formulation (F2) was calculated and the results obtained are represented in table 16.

Table 16. Release kinetics and mechanisms of Risperidone buccal tablet of optimized formulation (F2)

| Formulation code | Zero order (R ²) | First order (R ²) | Higuchi (R ²) | Hixon-Crowell (R ²) | Korsmeyer-Peppas | | Possible drug release mechanism |
|------------------|------------------------------|-------------------------------|---------------------------|---------------------------------|-------------------|--------|---------------------------------|
| | | | | | (R ²) | N | |
| F1 | 0.9908 | 0.911 | 0.9835 | 0.799 | 0.9465 | 0.6798 | Non-Fickian transport |

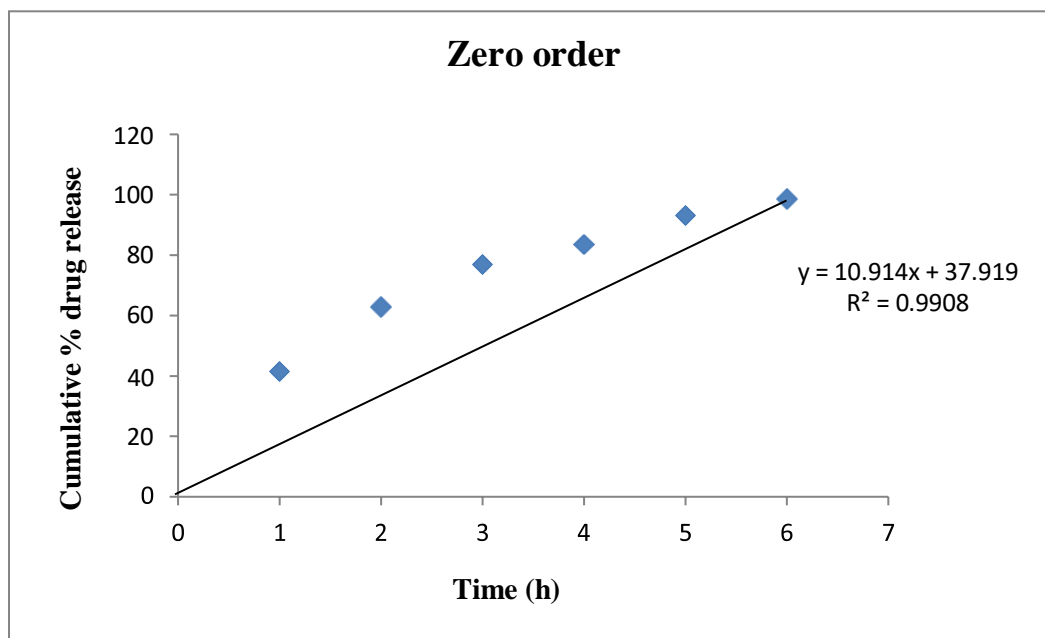


Fig. 9. Zero order profile for optimized formulation F2

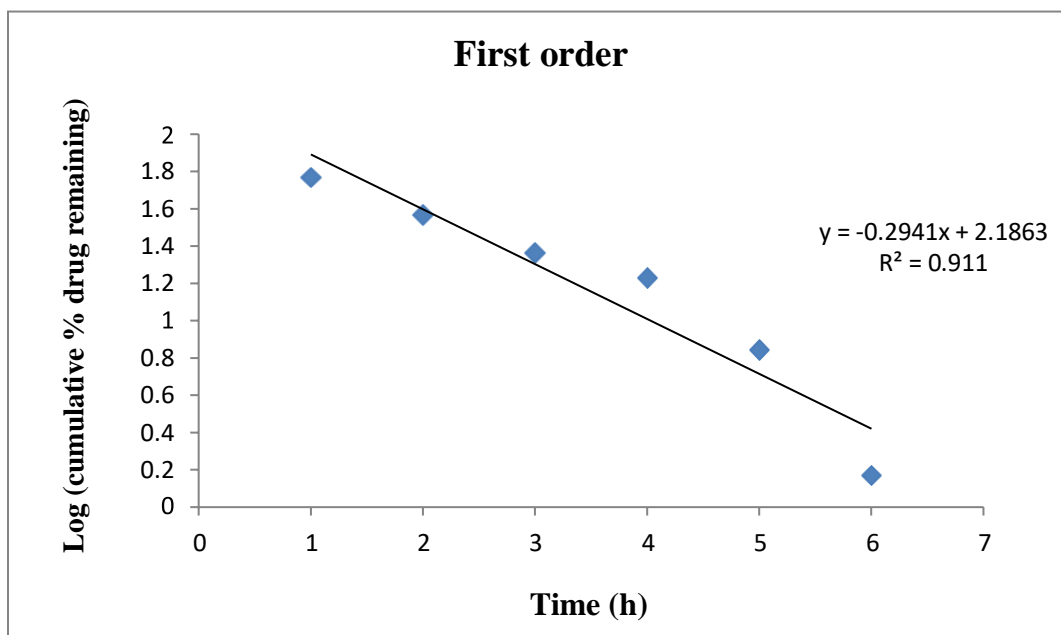


Fig. 10. First order profile for optimized formulation F2

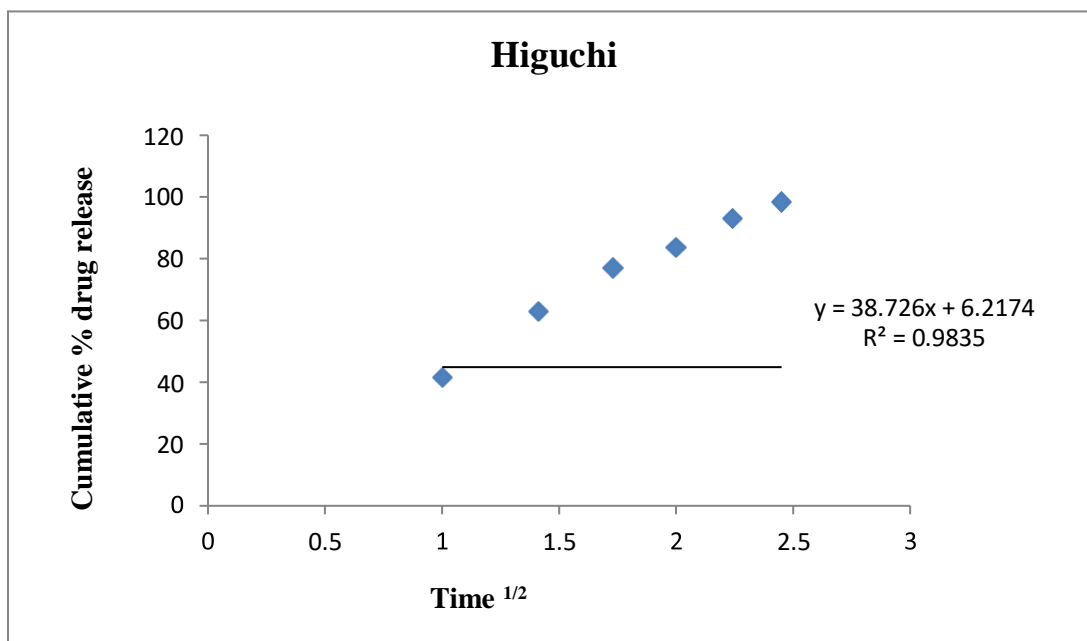


Fig. 11. Higuchi profile for optimized formulation F2

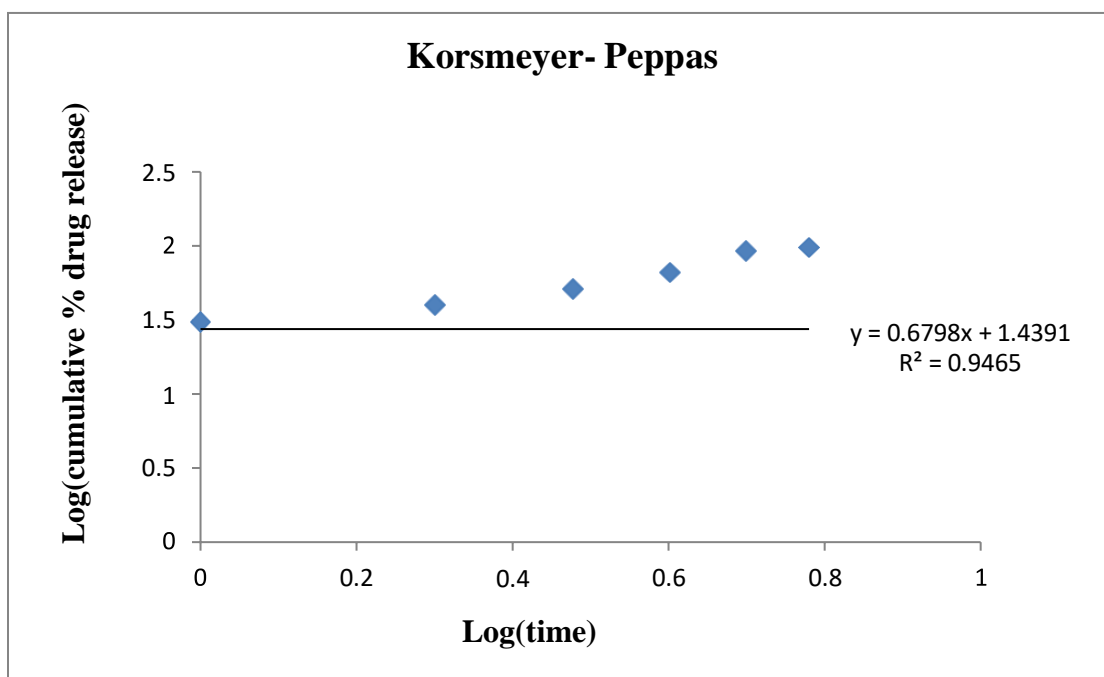


Fig. 12. Korsmeyer- Peppas profile for optimized formulation F2

DISCUSSION

Precompression formulation parameters

The standard calibration of pure drug proved that Risperidone supplied was of pharmacopoeia standards.

From the obtained FTIR peaks it can be concluded that the physical mixture of the drug Risperidone does not show any major interactions with formulation excipients.

Weight variation

Values of weight variation are found to be within the permissible limits of conventional oral tablets stated in the I.P.

Weights of the tablets varied between 97.3-102.1mg with deviation in the range of 1.91-3.62

The extreme variation could have been the result of mishandling of the tablet weights during punching process.

Thickness

The average thickness of Risperidone buccal tablets is found to be quite uniform with minimum variation.

The thickness of various tablet preparation were observed in the range of 2.60mm to 2.98mm with standard deviation in the range 0.023 to 0.091.

The thickness of the tablet and hence its total weight

must be appropriate in order to obtain good mucoadhesion, as the mucoadhesive property is also dependent on the geometry of the dosage form.

Hardness and friability

The hardness of the prepared Risperidone buccal tablet lies in the range of 3.24 to 4.02 g/cm² with the standard deviation in the range of 0.09 to 0.55.

Also the friability lies in the range of 0.025% to 0.520% Friability is not more than 1% for any formulation.

The hardness of Risperidone buccal tablets is low, but the friability data suggests that the tablets are quite robust enough to withstand the normal handling.

Surface pH

The surface pH of all the tablets is within the range of 6.58 to 7.01 which is close to neutral pH. There is negligible or no change in the surface pH of the tablets. Hence, no irritation to the buccal cavity is assumed.

Swelling Index

The result of swelling study reveals that the swelling index of all the tablets increases with time because the polymer gradually absorbs water due to hydrophilicity of the polymer.

Appropriate swelling behavior of mucoadhesive buccal system is essential for uniform and prolonged drug release and effective mucoadhesion.

The swelling index after 6 h. is in the range from 16.92 to 41.37% for formulation containing carbopol 943 with PVP 30, while for buccal tablets containing carbopol 934 with xanthan gum, it was in the range from 19.21-43.42%.

The swelling index is directly proportional to the concentration of second polymer (i.e. PVP 30 or xanthan gum) and inversely proportional to carbopol. The formulation containing higher levels of the second polymers (PVP K30 and Xanthan gum) displays the highest swelling index.

The reason for this is, they are of lower viscosity grade and hence the water penetration into the tablet matrix is facilitated by them or in other words, they are having a faster rate of water uptake.

***In vitro* drug release**

All the formulation shows good release (i.e.>85%)

For formulation F1, F2, F3 (containing carbopol and PVP 30) the drug release is found in the range of 78.23±0.7% to 98.25±1.2%

On the other hand formulation F4, F5, F6 (containing carbopol and xanthan gum) the drug release is found in the range of 81.34±1.5% to 96.54±0.2%

It can be concluded that an increase in carbopol content delays the drug release from the tablets.

Also the formulation which showed highest swelling index also exhibit high extent of drug release.

This may be due to the fact that the higher amount of water uptake by the polymers may lead to considerable swelling of polymer matrix, allowing the drug to diffuse out at a faster rate.

***Ex-vivo* drug permeation study**

For formulation F1, F2, F3 (containing carbopol and PVP 30) the cumulative percentage drug diffusion is found in the range of 72.63±2.1% to 96.63±1.4%.

Whereas formulations F4, F5, F6 (containing carbopol and xanthan gum) the drug release is found in the range of 79.54±1.8% to 95.81±0.6%.

From the data obtained from diffusion study, it can be concluded that higher level of carbopol retards the release from buccal tablet.

Whereas formulation containing higher level of second polymer (PVP K30 and Xanthan gum) showed a higher extent of drug diffusion.

***Ex- vivo* muco adhesion time**

The ex-vivo mucoadhesion time for the prepared buccal tablets varies from 5 h to more than 6 h.

The difference between the values of the ex-vivo mucoadhesion time for buccal tablets can be attributed to the combination of the various amounts of the polymer which affect the mucoadhesion.

Moreover, PVP K30 and xanthan gum owing to its solubility in water and the observed high swelling rate and extent, resulted in lower mucoadhesion time.

Whereas, tablets containing high proportion of carbopol, mucoadhesion time is found to be increased.

Drug release kinetics

Examination of the correlation coefficient (R^2) value indicated that the drug permeation followed a diffusion-controlled mechanism for the buccal tablet of best formulation (F2) as the R^2 value for zero order plot (0.9908) was higher in comparison to the first-order (0.911), Higuchi plot (0.9835), Korsmeyer Peppas plot (0.9465) and Hixson-Crowell plot (0.799) kinetic models, as shown in Table 23. The drug release is independent of concentration. Also, the n value of Korsmeyer-Peppas lies within $0.45 < n < 0.89$, which indicates that it undergoes anomalous diffusion or non-fickian diffusion.

Pharmacokinetic and pharmacodynamic studies in human beings.

CONCLUSION:

The oral cavity and its highly permeable mucosal tissues have been taken advantage for decades as a site of absorption for delivery of drugs to the systemic circulation. So the formulations which target the oral cavity through buccal mucosa are of considerable interest to improve the bioavailability and reduce the frequency of administration of APIs.

Drugs administered through the buccal route have a rapid onset of action and leads to improved bioavailability of drugs. The buccal route can bypass the first-pass metabolism, bypass contact of the drugs with the gastrointestinal fluids and paves way for easy access to the membrane sites so that the delivery system can be applied, localized and removed easily. Furthermore, there is good potential for prolonged delivery through the mucosal membrane within the oral mucosal cavity. Buccal adhesive systems offer

innumerable advantages in terms of accessibility, administration and withdrawal, retentivity, low enzymatic activity, economy and high patient compliance. Adhesions of these drug delivery systems to mucosal membranes lead to an increased drug concentration gradient at the absorption site and therefore improve bioavailability of systemically delivered drugs.

The research work highlights the development and evaluation of novel buccal drug delivery system of Risperidone so that the non-invasive administration of injection as well as gastrointestinal side effects of the drug (when administered orally) can be avoided.

At the current global scenario, scientists are finding ways to develop buccal adhesive systems through various approaches to improve the bioavailability of drugs used orally by manipulation of the formulation strategies like inclusion of pH modifiers, enzyme inhibitors as well as permeation enhancers.

REFERENCES:

- Gilhotra R.M., Ikram M., Srivastava S., Gilhotra N. A clinical perspective on mucoadhesive buccal drug delivery systems. *J. Biomed. Res.* 2014;28(2):81–97. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
- Gandhi A. Mouth dissolving tablets: a new venture in modern formulation technology. *Pharma Innov.* 2012;1(8):14–31. [[Google Scholar](#)]
- Bhowmik D., Chiranjib B., Pankaj K., Chandira R.M. Fast dissolving tablet: an overview. *J. Chem. Pharm.* 2009;1(1):163–177. [[Google Scholar](#)]
- Reddy P.C., Chaitanya K.S., Rao Y.M. A review on bioadhesive buccal drug delivery systems: current status of formulation and evaluation methods. *DARU J. Pharm. Sci.* 2011;19(6):385–403. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
- Shaikh R., Singh T.R.R., Garland M.J., Woolfson A.D., Donnelly F.D. Mucoadhesive drug delivery systems. *J. Pharm. Bioall. Sci.* 2011;3(1):89–100. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
- Alexander A., Ajazuddin S., Tripathi D.K., Verma T., Mayura J., Patel S. Mechanism responsible for mucoadhesion of mucoadhesive drug delivery system: a review. *Int. J. Appl. Biol. Pharmaceut. Technol.* 2011;2(1):434–445. [[Google Scholar](#)]
- Asane G.S., Nirmal S.A., Rasal K.B., Naik A.A., Mahadik M.S., Rao Y.M. Polymers for mucoadhesive drug delivery system: a current status. *Drug Dev. Ind. Pharm.* 2008;34(11):1246–1266. [[PubMed](#)] [[Google Scholar](#)]
- Madhav N.V., Shakya A.K., Shakya P., Singh K. Orotransmucosal drug delivery systems: a review. *J. Contr. Release.* 2009;140(1):2–11. [[PubMed](#)] [[Google Scholar](#)]
- Smart J.D. Buccal drug delivery. *Expet. Opin. Drug. Deliv.* 2005;2(3):507–517. [[PubMed](#)] [[Google Scholar](#)]
- Shanker G., Kumar C.K., Gonugunta C.S.R., Kumar B.V., Veerareddy P.R. Formulation and evaluation of bioadhesive buccal drug delivery of tizanidine hydrochloride tablets. *AAPS PharmSciTech.* 2009;10(2):530–539. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
- Çelik B. Risperidone mucoadhesive buccal tablets: formulation design, optimization and evaluation. *Drug Des. Dev. Ther.* 2017;11:3355–3365. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
- Boddupali B.M., Mohammed Z.N.K., Nath R.A., Bhanji D. Mucoadhesive drug delivery system: an overview. *J. Adv. Pharm. Technol. Res.* 2010;1(4):381–387. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]