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Formulation And Evaluation Of Buccal Film Of Antiperkinson Disease

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Abstract

The main objective of present investigation to formulate and evaluate mucoadhesive buccal patches of Levodopa, using solvent casting method. HPMC K100 M were used as a mucocoadhesive polymer and PEG 400 used as a plasticizer as well as penetration enhancers.

The formulated patches of Levodopa were evaluated for their appearance, weight variation, thickness, folding endurance, surface pH, swelling index, drug content, % elongation, mucoadhesive strength, in vitro drug release, kinetic release study and stability study. Among all formulated batches (S1-S8) of buccl patches batch S6 showing maximum drug release after 8 hours 94.77 % and mucoadhesive strength 10.21±0.35g). The stability study optimized batch S6 doesn't show any changes with respect to previous evaluation carried out before stability study. It may concluded the mucoadhesive buccal patches of Levodopa were successfully prepared using HPMC K100 M by solvent casting method, evaluated & it is better alternative to conventional drug delivery for the management of pain and arthititis

Keyword - buccal film , mucoadhesive , hpmc , levodopa

1. Introduction

Disease – parkinson's disease

Parkinson's disease (PD) is a common neurodegenerative disease. Early concepts looking at PD as purely a motor disorder have led the way to seeing it as a much more widespread neurological disease with affective, cognitive, and autonomic manifestations. The etiology of PD is still unknown, but important steps have been made to understand its pathogenesis. To a large extent, these derived from the identification of genetic variants of PD. Mutations in several genes have been discovered that cause monogenic PD, while GWAS has identified other loci associated with sporadic disease.

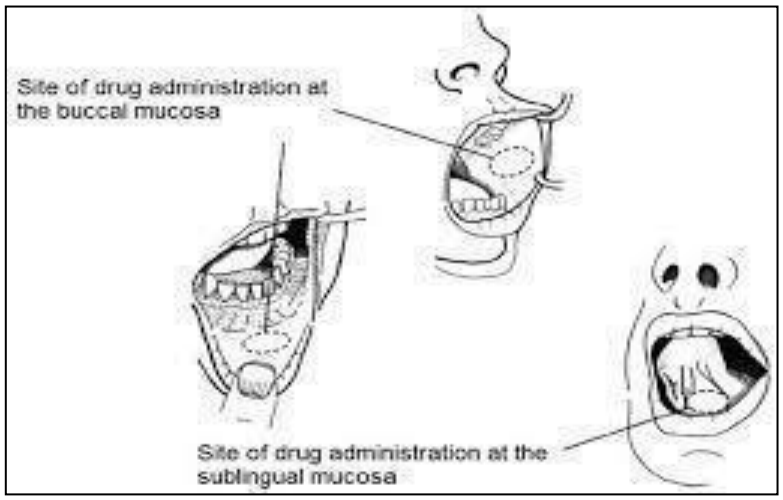
Several drugs are now available for the treatment of PD patients. These include drugs specifically aimed at

motor symptomatology (levodopa, dopamine agonists, monoxides B inhibitors, and amantadine) and agents for treatment of cognitive, affective, and autonomic manifestations. Levodopa is undoubtedly the most efficacious known agent to treat the motor dysfunction, but it has short-term and long-term adverse effects, limiting its use. Therefore, treatment of the initial stages of PD usually starts with dopamine agonists or with monoamine oxidase inhibitors. Anticholinergic drugs, once the mainstay therapy of PD, are now rarely used, except for the control of tremor. As the motor symptoms are relatively efficiently controlled, the non-motor symptom.

Parkinson's disease (PD), one of the most frequent neurodegenerative disorders, is a multiorgan proteinopathy characterized clinically by rigidity, akinesia, rest tremor, postural instability, and heterogenous nonmotor symptoms owing to a spreading process of synaptic and neuronal loss, due to deposition of misfolded a-synuclein (aSyn), the major protein marker of PD, and other synucleinopathies. Morphological features of PD are degeneration of the dopaminergic nigrostriatal system responsible for the core motor deficits and multifocal involvement of the nervous system and other organs associated with widespread occurrence of intracytoplasmic Lewy bodies and dystrophic neurites. The resulting striatal dopamine deficiency and multiple other biochemical deficits result in the heterogenous clinical picture of PD. Recent research has provided insights into the genetics, development, staging, and prion- like spreading of say, its relation with Lewy pathology, and clinical symptoms.

1.1 Buccal film

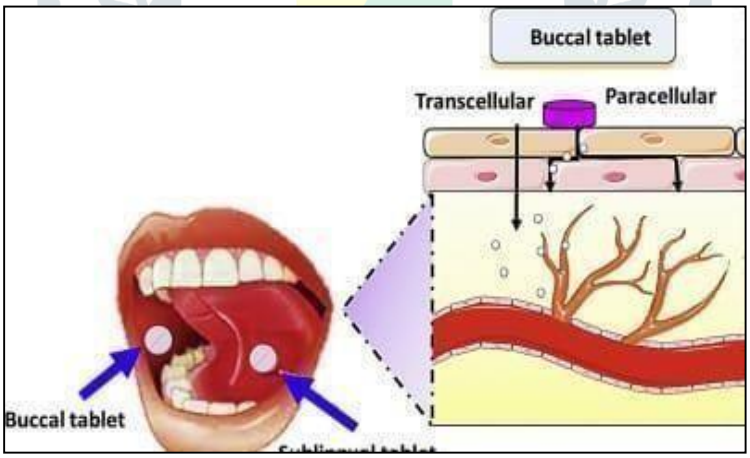
Buccal film is a non-dispersible thin type of spreadsheet modified release dosage form made up of one or more polymer matrix or coverings that holds the medicine and/or additional excipients.When relative to other dosage forms, the buccal film is an exquisite and effective dosage form with enhanced bioavailability since it skips hepatic first pass metabolism. Due to its tiny size, modest dose, and film thickness, it is the most agreeable and appetizing dosage form. Oral mucosa, teeth or gingiva may get adhered due to the presence of mucoadhesive polymers in the film. This enhances oral cavity getting appropriate medication release leading to produce better therapeutic effects which is defined as unidirectional release, individually in the oral cavity by unidirectional release or the two of them together i.e., bidirectional release. After a set amountof time, the patch is removed from the mouth and discarded.[9]



(fig: 1) Buccal film

1.2 Mechanism of buccal absorption

A slow dispersion of non-isolated or individual species results in better buccal absorption of drugs. Concentration gradient plays a wide role in regulation of the entire process through intertwined epithelium spaces. Transmission of non-ionic species throughout the buccal lipid membrane is the primary mode of transport. The buccal mucosa is said to be a lipoidal barrier to drug overdose, as it does in many other mucosal pores and where the drug molecule is lipophilic,it is where it is most easily absorbed.23 The dynamics of buccal drug absorption can be adequately explained by the first dose procedure. Dearden and Tomlinson (97) have shown that saliva begins to change buccal absorption kinetics from drug solution by doing significant changes and alterations of the drug overload in the mouth. The correspondence between saliva and time is given as follows:[10]



(fig: 2) mechanism of buccal film

2. Material and methods

Material

Ingradient

- Drug- Levodopa
- Plasticizer- Methanol
- Polymer - HPMC
- Polyester -Propylene glycol
- Additive - Citric acid

Equipment

- Beaker
- Measuring cylinder
- Petri dish
- Stirrer
- Analytical balance
- Solvent casting machine

Table no : 1 ingradient

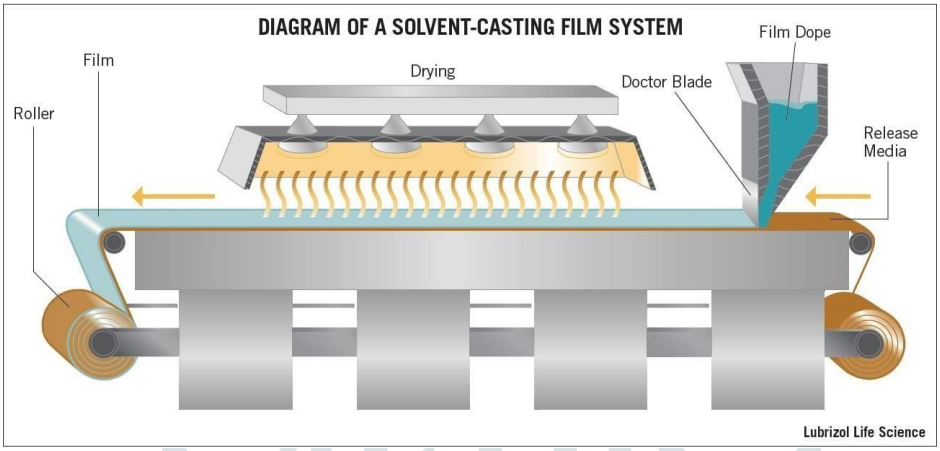
ngredients	Quantity
evodopa	gm
Methanol	0 ml
HPMC	gm
Propylene glycol	gm
Citric acid	gm

Method

1. Solvent casting method

The films were prepared at room temperature with the solvent casting method.

Figure 1



(fig: 3) solvent casting film system

A process for solvent casting including, casting a dope from a casting die onto a casting support, drying the cast dope on the casting support to form film, stripping off the film from the casting support, and further drying the film, wherein the dope has a solid matter content of from 17 mass % to 30 mass %, and a mean drying rate between the casting of the dope and thestripping off is more than 300 mass %/minute and not more than 1000 mass %/minute. Also, aprocess for solvent casting including the steps of casting a dope from a casting die to a casting support, forming the film by drying the dope to some extent, stripping off the film from the casting support and further drying the film while conveying the film with carrying it at both side edges of the film by a tenter under specified conditions.

A process for solvent casting which comprises casting a dope from a casting die onto a castingsupport, drying the cast dope on the casting support to form a film, stripping off the film from the casting support, and further drying the film while conveying the film with carrying it at both side edges of the film by a tenter, wherein dry thickness (X μm) of the both side edges and mean dry thickness (T μm) of product portion of the film have following relationship.[26]

Formulation of buccal film

Procedure

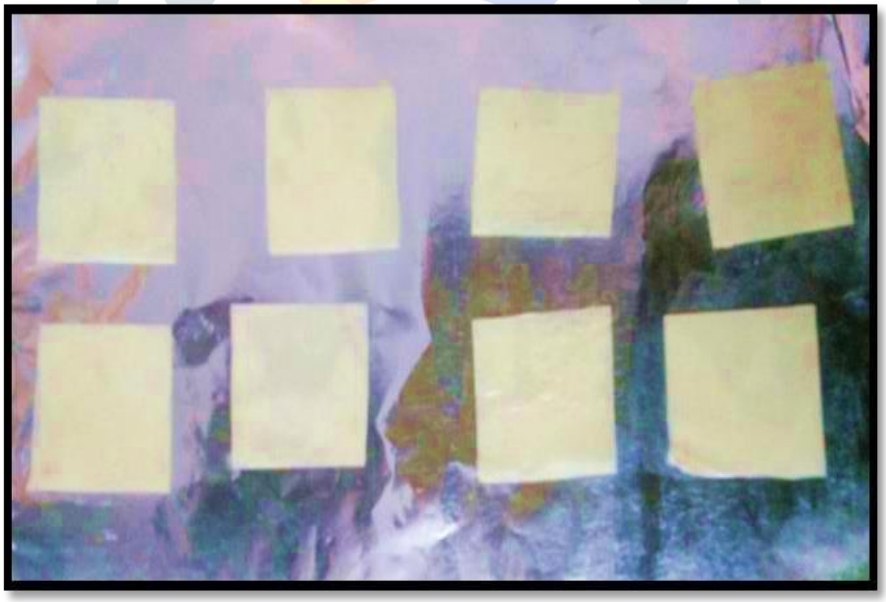
- The first step of preparation, methanol (1, 1.5, 2 w/w %) was dissolved in distilled water and mixed (900 rpm) at room temperature with an overhead stirrer.

- The second step of mixing speed of the solution was decreased (500 rpm) and levodopa was incorporated in the polymer solution (0.0793 w/w%) for 5 h.

- As the third step, HPMC (1, 1.5. 2 w/w%) was added to the solution with mixing.

- In the fourth step, propylene glycol and citric acid was added to the solution. Mixing was stopped and it was placed in an ultrasonic unit for 30 min to help the number and the size of air bubbles reduce and remove from the solution.

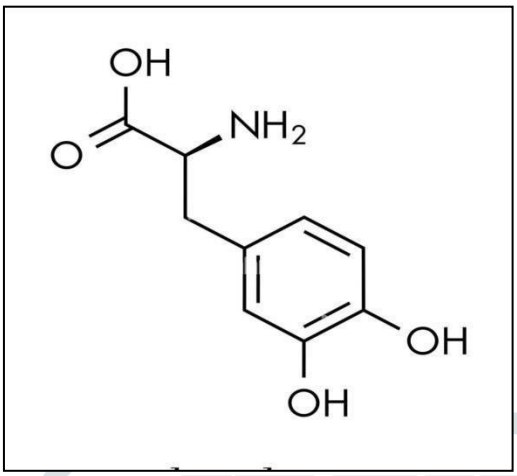
- The solution (pH = 6.7–7.0, viscosity: 140–173 mPa•s) was cast onto a glass surface in Petri dishes (7.6 cm diameter), with 10 g of solution/dish, then it was dried at room temperature (24.4 ± 0.5 ◦C). The dried polymer films were removed from the surface and placed in closed containers (24.4 ± 1 ◦C, 60 ± 2% RH). the camera photos of Sample 4 (1.5% propylene glycol
+ 1.5% HPMC+ 1% propylene glycol) can be seen. [27]



(fig: 4) formation of buccal film

4. Drug Profile

Levodopa



Description

- IUPAC Name - 2-amino-3-(3,4 dihydroxyphenyl) propanoic acid
- Molecular Formula - C9H11NO4
- Molecular Weight - 197.188
- Melting Point - 396.26 [°C]
- Appearance - peach to light peach coloured with mosaic appearance, oval shaped,
- Identification - UV Spectroscopy
- Log P - 0.05
- Category - Levodopa is in a class of medications called central nervous system agents
- Solubility - It is slightly soluble in ethanol (95), and practically insolu- ble in water and in diethyl ether. It dissolves in sodium hydroxide TS. It is gradually colored by light.

5. Evaluation Test

Weight Uniformity of film:

Weight variation is studied by individually weighing 3 randomly selected films and by calculating the average weight.[29]

Thickness of films:

The thickness of film is determined by micrometer screw gauge at 5 different points of the film i.e central and the four corners and means thickness is calculated. For measurement of Uniformity of thickness, 5 film are randomly selected and thickness is measured on location of each formulation Maximum variation in the thickness of the films should be less than 5% and mean ±S. D. is calculated.[30]

Folding Endurance of film:

Folding endurance is measured by manually repeated foldingof film at same place till it broke. The number of time the film is folded without breaking is known as the folding endurance value.The flexibility or elasticity of film can be measured. Folding endurance was measured by manually or practically for the prepared films. Take a 2X2cm films and folded repeatedly at the same place till it broke. The no times the film could be folded at the same place withoutbreaking gave the exact valve of folding endurance.[31]

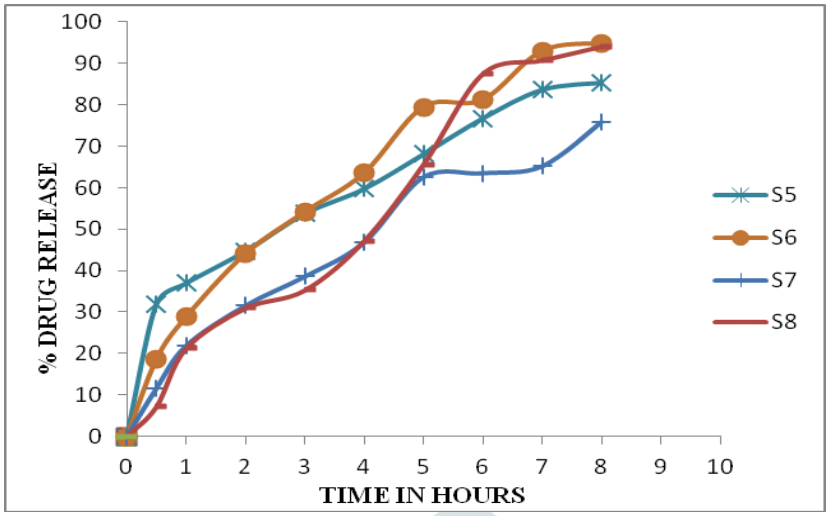
Surface pH of film:

The film to be tested was placed in a petridish and was moistened with 1ml of distilled water and kept for 30s. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1min. The average of three determinations for each formulation was done.[32]

.In vitro Drug Release:

The release rate of the levodopa fast dissolving film was determined by the help of USP Dissolution Test Apparatus-II. The dissolution test was performed using 300 ml PhosphateBuffer Solution pH 6.8, at 37 0.50C with 50 rpm of the paddle speed. Aliquot 5 ml of thesolution was collected from the dissolution apparatus at time interval of 1 min and at the sametime add 5 ml or same amount of fresh dissolution medium. The Aliquot filtered through thewhatman filter paper. The absorbance of the filtered solution was measured at 290 nm.

The aliquot should be withdrawn at the zone between the surface of the dissolution medium and the top of rotating paddle not less than 1 cm apart from the vessel wall. Cumulative percent drugrelease can be calculated by using the equation obtained from the standard curve or % drug release formula. [33]



Disintegration time:

The disintegration time limit is of 5 min or less for orally disintegrating tablets, as described in CDER guideline and can be applied to fast dissolving oral film. No official guideline is available for oral fast dissolving films. Pharmacopoeia disintegrating test apparatus may be used for this study. Typical disintegration time for film is 2 to 3 min.[34]

Stability study

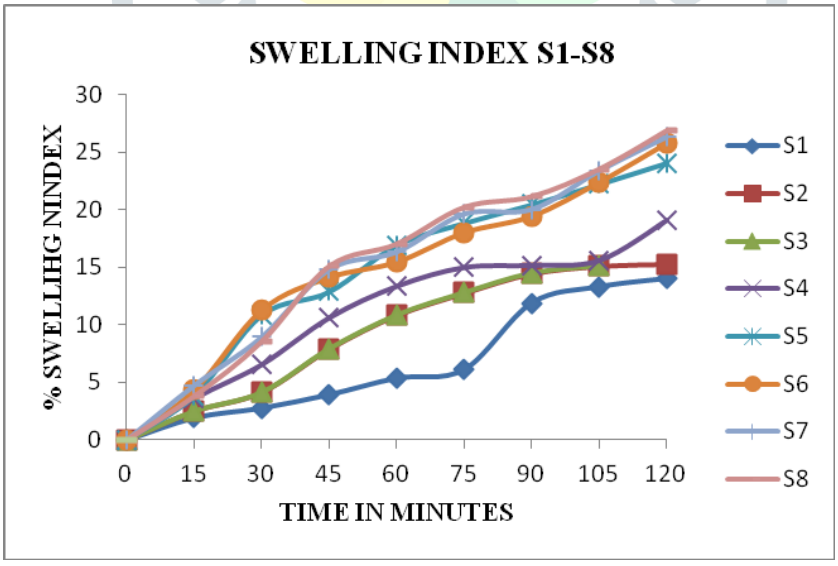
Formulation batch S6 has shown best results amongst all 8 batches. So stability study was carried out on formulation batch S6. Different patches were kept in on 40 ^{0}C with 75% respectively for the period of three months and evaluated after three months.[35]

Swelling Index

The percentage swelling index taken at predetermined time intervals of 15minutes to 90 minutes for trial batches and 15 minutes for 120 minutes for final batches. The calculated percentage swelling.[36]

Table No. 2: SWELLING INDEX OF FORMULATED BATCHES.

Time (min)	Percentage of Swelling (%)							
	S1	S2	S3	S4	S5	S6	S7	S8
0	0	0	0	0	0	0	0	0
5	1.92	2.50	3.61	3.86	4.33	4.73	3.80	3.88
0	2.77	4.14	6.56	0.86	1.28	8.03	8.55	8.08
5	3.93	7.91	0.63	2.89	4.12	4.79	5.08	5.08
0	5.36	0.83	3.37	6.93	5.46	6.31	7.01	6.94
5	6.12	2.77	5.00	8.85	8.02	9.60	0.20	0.59
0	1.88	4.46	5.18	0.46	9.44	0.00	1.12	1.93
05	3.28	5.10	5.61	2.24	2.40	3.35	3.51	3.97
20	3.99	5.29	9.11	4.08	5.79	6.29	6.85	6.33



6. Result and discussion

The study results indicate that levodopa buccal films offer a distinct advantage over traditional oral tablets in terms of rapid onset of action and improved bioavailability. The faster absorption through the buccal mucosa bypasses the gastrointestinal tract, which can be particularly beneficial for patients experiencing delayed gastric emptying, a common issue in Parkinson's disease.[37]

Levodopa buccal films represent a promising advancement in the treatment of Parkinson's disease, offering rapid symptom relief, improved bioavailability, and a favorable safetyprofile. This novel delivery system could become a valuable addition to the therapeutic arsenal for managing Parkinson's disease, particularly for patients requiring quick and reliable symptomcontrol.

Absorption Rate: The buccal film showed a faster absorption rate compared to oral tablets, with a peak plasma concentration (C_max) reached within 1-2 minutes.

7. Conclusion

In the present study, the buccal films of levodopa were prepared successfully by solvent casting method. The optimized buccal film (F6) composed of drug: HPMC E15 (1:10) in methanol mixture along with as plasticizer and 0.6% citral as permeation enhancer showed satisfactory physicochemical properties,good physical stability, highest percent drug release and followed zero order model of drug release and fairly good amount of drug permeation through the porcine buccal membrane in 8hrs. The formulation F6also showed significantly high times more than that of drug suspension. Hence, the present study concludes that these erodible F6 buccal filmsof levodopa can be very promising for effective doses to systemic circulation circumventing the hepatic first pass metabolism and enhances bioavailability

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