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FORMULATION & EVALUATION OF AMLODIPINE BUCCAL FILM: A NOVEL APPROACH FOR THE TREATMENT OF HYPERTENSION

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ABSTRACT: Hypertension, a prevalent cardiovascular condition, presents significant health risks worldwide. This abstract provides a concise summary of hypertension, encompassing its definition, prevalence, risk factors, and implications. It elucidates the physiological mechanisms underlying hypertension, emphasizing its multifactorial nature, including lifestyle factors, genetics, and environmental influences. The abstract also discusses the importance of early detection and management strategies, highlighting lifestyle modifications and pharmacological interventions. Understanding hypertension's impact on cardiovascular health is crucial for public health initiatives aimed at prevention and control. This overview serves as a foundational guide for healthcare professionals and individuals alike in combating the global burden of hypertension. Amlodipine Besylate is a calcium channel blocker class antihypertensive drug. Which is used to treat the hypertension with the combination of other drugs but the patient who are suffering from the gastric or hepatic related problem then the solid form of this drug shows very less effects. The main aim of this research is formulation and evaluation of Amlodipine buccal films to avoid first pass metabolism and enhance bioavailability

Keywords: Hypertension, Amlodipine Besylate, first pass metabolism, antihypertensive drug, calcium channel blocker, buccal films.

1. Hypertension

Hypertension (high blood pressure) is when the pressure in your blood vessels is too high (140/90 mmHg or higher).It is common but can be serious if not treated. People with high blood pressure may not feel symptoms. The only way to know is to get your blood pressure checked Worldwide, 1.28 billion persons between the ages of 30 and 79 are projected to have hypertension Adults with hypertension are reportedly 46% less likely to be aware of their condition. Hypertension may be classified into primary and secondary:

1.1 PRIMARY HYPERTENSION

It is otherwise known as essential hypertension. It is characterized by the following:

- Elevation of diastolic BP.
- Normal cardiac output.
- An increase in peripheral resistance.

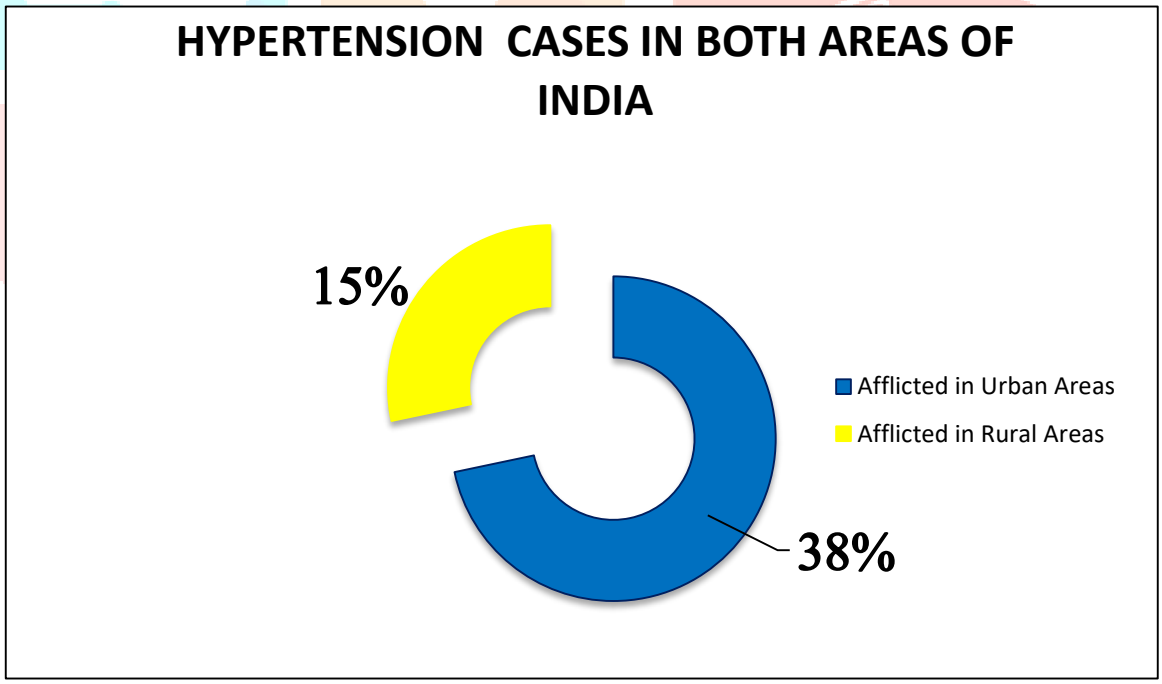

Figure 1: Hypertension cases in both areas of India

1.2 SECONDARY HYPERTENSION

Factors causing secondary hypertension are as follows:

- Acute or chronic renal disease.
- Hyperaldosteronism.
- Cushing's syndrome.
- Acromegaly.
- Pheochromocytoma.
- Oral contraceptives, steroids, estrogen, and sympathomimetics

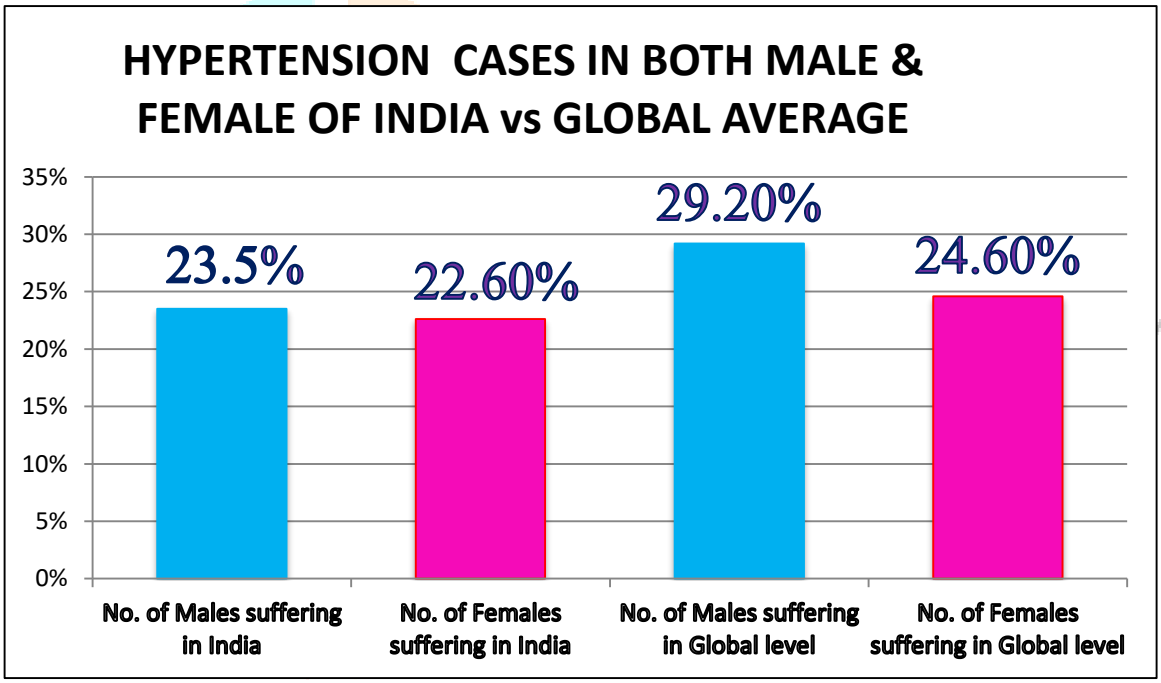

Figure 3: Hypertension cases in both male & female of India vs Global average

Causes:-

» Overweight

» Smoking

» Lot of stress

» Do not do exercise

» Eat too much salt

» Drink too much alcohol or coffee or other caffeine-based Drinks.

Prevention:-

» Eat a Healthy Diet

» Keep Yourself at a Healthy Weight

» Be Physically Active

» Do exercise

» Do Not Smoke

» Get Enough Sleep.

» Choose healthy meal

But still hypertension can't be control after suffering from it , so we required some medication to treat this disease.

2. **Antihypertensive drug**

Antihypertensive drug therapy has improved remarkably in the last 50 years. Before 1950, less effective and less tolerated antihypertensive drugs were available. Veratrum and sodium thiocyanate could lower BP, but were toxic and difficult to use. The ganglion blockers that were developed in the 1950s were effective, but inconvenient. Reserpine was a breakthrough, but produced mental depression. The therapeutic potential of hydralazine was not tapped fully because of the marked side effects when it was used alone. Guanithidine introduced in 1961 was an improvement on the ganglion blockers. The antihypertensives of 1960–70s were methyldopa, β-blockers, thiazides, high-ceiling diuretics, and clonidine. The antihypertensive of 1980–90s are angiotensin II converting enzyme inhibitors and calcium channel blockers. Angiotensin receptor blockers (losartan) are the latest antihypertensives. Diuretics and related drugs are the choice in uncomplicated hypertension. These drugs reduce plasma and extra cellular fluid volume by 5%–15% that decrease cardiac output. The reduction in total peripheral resistance is most probably an indirect consequence of small persisting Na+ and volume defect. Decreased intracellular Na+ concentration in the vascular smooth muscle may decrease stiffness of vessels wall, increase compliance, and dampen responsiveness to constrictor stimuli of noradrenaline and angiotensin II. Angiotensin-converting enzyme (ACE) inhibitors are one of the first choice drugs in all the grades of essential as well as reno-vascular hypertension. When it is used alone, 50% of the patients are benefited and the addition of a diuretic/β blocker extends the efficacy to 90%. Angiotensin receptor blockers give peak action at 2–4 weeks. Calcium channel blockers such as dihydropyridines, phenylalkylamine, and benzothiazepine are equally effective antihypertensives. Beta adrenergic blockers give 30%–40% efficacy in mild-to-moderate cases.

3. **CALCIUM CHANNEL BLOCKERS**

Calcium channel blockers (CCBs) are another class of first line antihypertensive drugs. All 3 subgroups of CCBs, viz. dihydropyridines (DHPs, e.g. amlodipine), phenyl alkylamine (verapamil) and benzothiazepine (diltiazem) are equally efficacious antihypertensives, but DHPs are mainly used. They lower BP by decreasing peripheral resistance without compromising c.o. Despite vasodilatation, fluid retention is in significant. Ankle edema that occurs in some patients is due to increased hydrostatic pressure across capillaries of the dependent parts as a result of reflex constriction of post capillary vessels in these vascular beds. The onset of antihypertensive action is quick. With the availability of long acting preparations, most agents can be administered once a day. Short acting CCBs/formulations (nifedipine regular formulation) are

not used to treat hypertension. Monotherapy with CCBs is effective in ~ 60% hypertensive, and they may improve arterial compliance. Other advantages of CCBs are:

1. Do not compromise haemodynamic: no impairment of physical work capacity.

2. No sedation or other CNS effects; cerebral perfusion is maintained.

3. Not contraindicated in asthma, angina (especially variant) and PVD patients: may

benefit these conditions.

4. Are particularly effective in elderly patients, black races and low renin hypertensives.

5. Do not affect male sexual function.

6. No deleterious effect on plasma lipid profile, uric acid level and electrolyte balance.

7. Shown to have no/minimal effect on quality of life.

8. No adverse foetal effects; can be used during pregnancy (but can weaken uterine contractions during labour).

4. About Fast dissolving drug delivery system (FDDS)

Fast-dissolving drug-delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties swallowing traditional oral solid dosage forms. In response to this need, a variety of orally disintegrating tablet (ODT) formats were commercialized. New treatment plans and medication is replacing other forms of treatment like psychotherapy, physical therapy, radiation therapy etc. These having an increasingly prominent role in the treatment and prevention of diseases in the population. The health of the citizens depends on the availability of safe, effective and affordable medicines. Each pharmaceutical company wants to formulate style such the novel oral dosage form, which has the higher bioavailability, quick action and most patient compliance. So, they formulate the fast dissolving tablets by using, super disintegrants and hydrophilic ingredients.

5. Criteria required for Fast dissolving films

» Require no water for oral administration, yet dissolve/disperse/disintegrate in mouth in

matter of seconds

» Have a pleasing mouth feel, to increase the patient compliance.

» Have an acceptable taste masking property.

» Subsequent to oral administration, it should leave least or no residue in mouth; this avoids the need of water.

» It should be compatible with the other ingredients, so that films can manufacture easily.

6. About Amlodipine besylate (ADB) buccal film

Amlodipine is highly lipophilic and almost completely absorbed after oral administration. However, it is extensively metabolized by the liver and an average, only about 30 to 60% of Amlodipine reaches the systemic circulation i.e. bioavailability of Amlodipine is very low. Hence to enhance its bioavailability, fast dissolving dosage form of amlodipine is formulated. Amlodipine falls under Class I of BCS classification i.e.

high solubility and high permeability. This means the drug can readily solubilize in saliva and permeate through GI mucosa. Via highly vascularized oral mucosa, the drug reaches systemic circulation. This dosage form apart from enhanced bioavailability also has other advantages like:

» Fast onset of action,

» Low amount of api to be incorporated to make the drug therapeutically active,

» Lower systemic side effects,

» Improved patient compliance etc.

Moreover, there is no requirement of any type of sophisticated equipment's and machines. So, Amlodipine buccal film is a medication delivery system designed to administer amlodipine, a commonly prescribed calcium channel blocker, through the buccal mucosa (inside of the cheek). This method offers potential advantages such as rapid absorption and avoidance of the gastrointestinal tract, which can be beneficial for certain patients. It's typically used for conditions like high blood pressure and angina.

7. Drug profile

The active substance is may be from any class of pharmaceutically active substances that can be administered orally or through the buccal mucosa respectively. According to literature, API can be added from 5%-25% w/w of total weight of polymer. For the effective formulation, dose of drug should be in mgs (less than 20 mg/day). The drugs which are potent, show high first pass metabolism and patient non- compliant are best candidates for fast dissolving buccal films.

Name of drug : Amlodipine Besylate

IUPAC name : 3-ethyl 5-methyl 2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate

Melting Point : 119-201^{o}C

Structure:

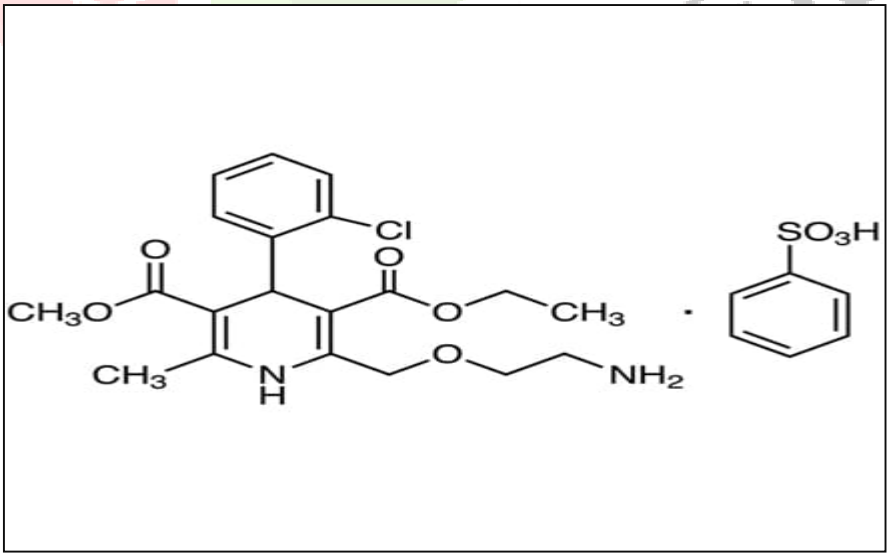

Fig 3 : Chemical Structure of Amlodipine Besylate molecule

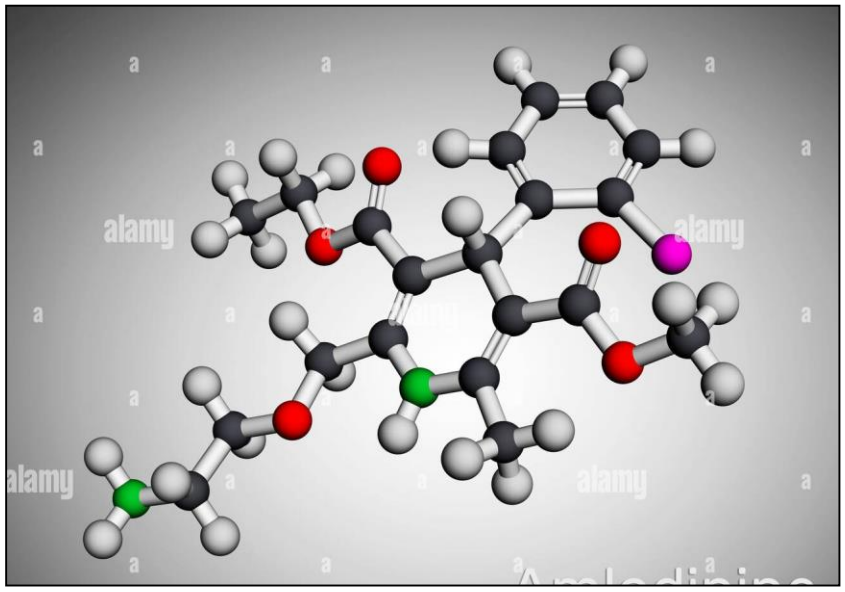

Fig 4: 3D Structure of Amlodipine Besylate molecule

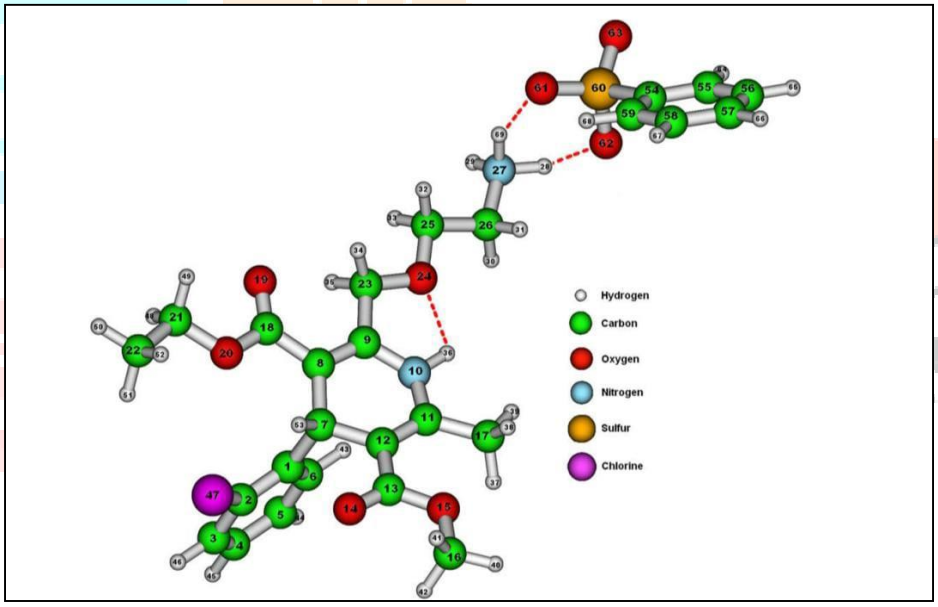

Fig 5: Optimized molecular structure and atom numbering scheme of Amlodipine besylate

Density : 1.2±0.1 g/cm^3

Boiling Point : 527.2.4±50.0 °C at 760 mmHg

Solubility : low water solubility (2.93 g/L)

Molecular weight: 408.879 g/mol

BCS classification: Class I

Class : Calcium channel blocker

pH : 1.2 (highly acidic)

8. Excipient profile

8.1. Polymer Forming Agent

A variety of polymers are available for preparation of fast dissolving buccal films. The polymers can be used alone or in combination to obtain the desired film properties. The film obtained should be tough enough so that there won't be any damage while handling or during transportation. The robustness of the strip depends on the type of polymer and the amount in the formulation. The various polymers to make fast dissolving films include cellulose or cellulose derivatives, pullulan, gelatin, hydroxypropylmethyl cellulose, hydroxyethyl-cellolose, hydroxypropylcellulose, polyvinylpyrrolidone, carboxymethylcellulose, polyvinylalchohal, sodium alginate, xanthine gum, tragacanth gum, guar gum, acacia gum, methylmethacrylate co-polymer and hypromellose are most commonly used for preparation of fast dissolving films. Modified starches are also used for preparation. Due to low cost of this excipient it is used in combination of pullulan to decrease the overall cost of the product. Pullulan is a natural polymer obtained from nonanimal origin and does not require chemical modification. About 50 to 80 percent w/w of pullulan can be replaced by starch in the production of fast dissolving films without loss of required properties of Pullulan. Combination of microcrystalline cellulose and maltodextrin has also been used to formulate fast dissolving films. Kulkarni et al., 2010 explored different polymers for use in formulation of oral fast dissolving strips. Different polymers viz., HPMC E15, HPMC K4M, HPMC E5, PVP, PVA, gelatin, eudragit RL100 and pullalan were used to formulate fast dissolving buccal films; by solvent casting method. Results confirmed that pullalan is best polymer for oral fast dissolving strips.

8..2. Plasticizers:

Plasticizer is a vital ingredient of the fast dissolving buccal films formulation. The mechanical properties such as tensile strength and elongation to the films can be improved by the addition of the plasticizer. It also helps to improve the flexibility of the strip and reduces the brittleness of the strip. They also improve the strip properties by reducing glass transition temperature of the polymer. The flow of polymer also gets better by the addition of the plasticizer. Variations in their concentration affect these properties. The selection of the plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in its casting. Plasticizers include glycerine, sorbitol, propylene glycol, polyethylene glycol, triacetin, di-butylpthalate, triethyl citrate, acetyl triethyl citrate and other citrate esters. Typically the plasticizers are used in the concentration of 0-20% w/w of the dry polymer weight. Inappropriate use of the plasticizer may lead to film cracking, splitting, peeling of the strip and it may also affect the absorption rate of the drug.

8.3. Surfactants:

Surfactants are used as solubilizing or wetting or dispersing agents so that the film gets dissolved within seconds and release active agent immediately. Surfactants also improve the solubility of poorly soluble drugs in fast dissolving buccal films. Some of the commonly used are polaxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and spans etc

8.4. Sweetening agents:

Sweeteners have become the important part of pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The classical source of sweetener is sucrose, dextrose, fructose, glucose, liquid glucose and isomaltose. The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol, and isomalt can be used in combination as they additionally provide good mouth-feel and cooling sensation. Polyhydric alcohols are less carcinogenic and do not have bitter after taste which is a vital aspect in formulating oral preparations. The artificial sweeteners have gained more popularity in pharmaceutical preparations. Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which fall under the second generation artificial sweeteners. Acesulfame-K and sucralose have more than 200 and 600 time sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. Rebiana which is a herbal sweetener, derived from plant Stevia rebaudiana (South American plant) has more than 200 -300 time sweetness

8.5. Saliva stimulating agents:

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strip formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them.

8.6. Flavouring agents:

Flavouring agents can be selected from the synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavours can be used alone or in the combination. Any flavor can be added such as essential oils or water soluble extracts of menthol, intense mints such as peppermint, sweet mint, spearmint, wintergreen, cinnamon, clove, sour fruit flavor such as lemon , orange or sweet confectionary flavours such as vanillin, chocolate ,or fruit essence like apple , raspberry, cherry, pineapple. The amount of flavor needed to mask the taste depends on the flavor type and its strength.

8.7. Colouring agents:

A full range of colours is available including FD& C colours, EU colours, natural colouring agents, and natural juice concentrates, pigments such as titanium oxide, silicon dioxide and zinc dioxide and custom pantone-matched colours. These all colouring agents should not exceed concentration levels of 1% w/w. these agents are incorporated when some of the formulation ingredients or drugs are present in insoluble or suspension form.

9. More Solubility Tests of ADB Drug:- For this we take 0.10gm of drug sample & dissolve into different solvents to determine the solubility of drug in different solvents. Amlodipine is soluble in organic solvents such as ethanol, DMSO (Dimethyl sulfoxide (DMSO) is a widely used solvent that is miscible with water and a wide range of organic solvents.), and dimethyl formamide (DMF). The solubility of amlodipine in ethanol and DMSO is approximately 12.5 mg/ml and approximately 20 mg/ml in DMF. Amlodipine is sparingly soluble in aqueous buffers.

S.No.	Solvent	Solubility of Drug Amlodipine	
		Observation	Standard
1.	Distilled Water	Poor soluble	Poor soluble
2.	Methanol	Freely Soluble	Freely Soluble
3.	Ethyl alcohol	Soluble	Soluble
4.	0.1M HCL	Freely Soluble	Freely Soluble
5.	Chloroform	Slightly soluble	Slightly soluble
6.	DSMO	Freely soluble	Freely soluble
7.	Benzene	Poor soluble	Poor soluble
8.	Acetic acid	Soluble	Soluble

Table No. 1; Solubility Tests of ADB Drug in different Solvents

10. Spectroscopic Studies of ADB Drug with UV- Spectroscopy: A simple, sensitive, specific, and validated UV method has been developed for the quantitative determination of Amlodipine besylate in pure and tablet dosage form. The λ max was found to be 365nm for assay. It is determined by Shimadzu 1900 – UV –Vis Spectroscopy.

10.1. Determination of λ max: A 100mg of Amlodipine Besylate was weighed accurately and dissolved in100mL Ethanol to obtain 1000 mcg per ml. this solution was subjected to double dilution of 10 ml with 100ml of ethanol to yield 10 pmm solution. The resulting solution is scanned between 200-400 nm and absorption maxima were determined. The above solution was diluted to 10 mcg/ml and scanned from 200-400 nm.

10.2. Linearity Curve (Calibration Curve): The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. Five serial concentration of standard drug is prepared. The absorbance of the resultant solutions is taken at absorption maxima. Calibration curve is prepared by plotting concentration versus absorbance for the various concentrations of drug medium.

Table No. 2; Determination of λ max by UV Analysis

S.No.	Observe λ max	Average λ max	Reference λ max
1.	365	365+364+366+365+365/ 5 1825/5 365	366
2.	364		
3.	366		
4.	365		
5.	365		

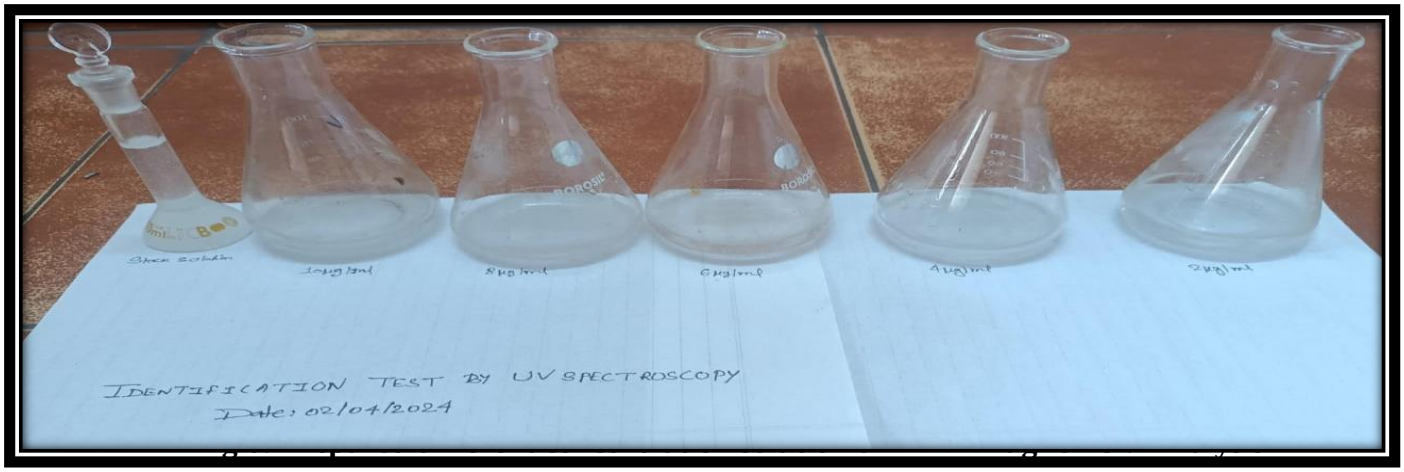

Fig 7: Determination of λ max of Amlodipine Buccal Film by UV- Spectroscopy

Table No. 3; Values of Calibration Curve of Amlodipine Besylate Drug

S. No.	Concentration(µg/ml)	Absorbance
1.	2	0.192
2.	4	0.259
3.	6	0.297
4.	8	0.325
5.	10	0.335

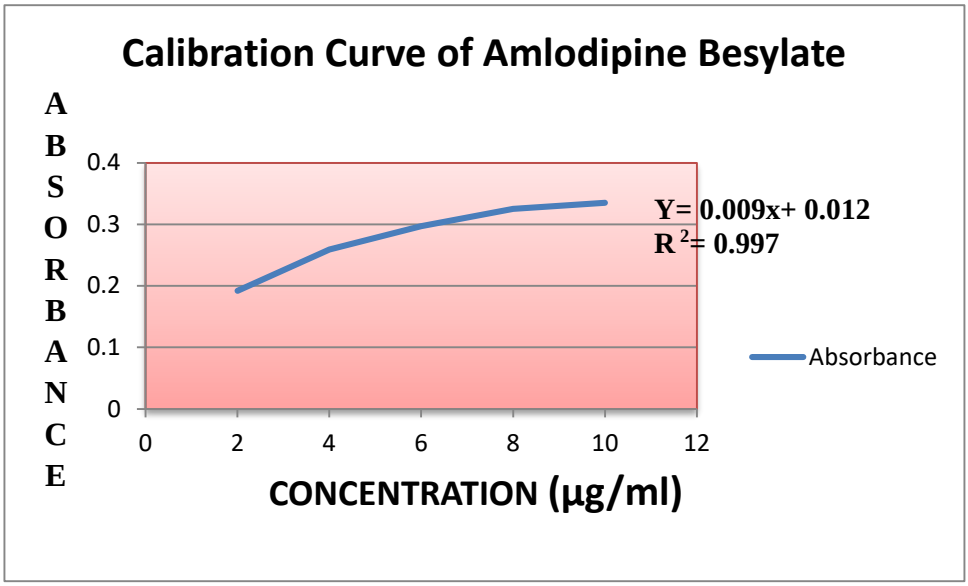

Fig 8: Calibration Curve of Amlodipine Besylate Drug

11. Materials used in preparation of ADB Buccal Films

11.1Active Pharmaceutical Ingredient (API):- Amlodipine Besylate

11.2 Excipients:-HPMC K_{100}, Distilled water, Ethanol, Food colour, Peppermint oil, Glycerol & Citric acid.

Table No.4: Composition of ADB Buccal Film

S. No.	Material	Quantity	Activity
1	Amlodipine Besylate	25mg (0.02g)	Antihypertensive agent
2	Distilled water/	15 ml	Solvent
3	Ethanol	5 ml	Preservative
4	HPMC	2 gm	Polymer
5	Food colour	q.s.	Colouring aent
6	Peppermint oil	q.s.	Flavouring agent
7	Glycerol	2 ml	Plasticizer
8	Citric acid	50mg (0.05g)	Saliva stimulating agent

12. Procedure for Preparation of ADB Buccal Films BY Solvent Casting Method:-

Firstly weigh all required ingredients

↓

Then dissolve Citric acid in distilled water in a beaker

↓

Add HPMC and Ethanol in the solution with continuous stirring

↓

Then add Glycerol and peppermint oil with stirring the solution

↓

Then add colouring agent in it with continues mixing

↓

Prepared solution is cast as a film and allows it to dry

↓

Collect the dry films and store it

13. Evaluation parameters of ADB Buccal Films:

13.1 Weight variation test:

Weight variation is obtained by individually weighing 08 randomly selected films each of 2 X 2 cm^2 and compared with the average weight for deviation.

Fig 18: Weight variation test for ADB Buccal Films

Table No.5: Weight variation test for ADB Buccal Films

No. of Sample of ADB Films	Weight of each ADB Films	Average
Sample 1	0.41gm	0.41gm +0.40gm +0.40gm+0.41gm +0.40gm+0.41gm +0.41gm +0.40gm / 8
Sample 2	0.40gm	
Sample 3	0.40gm	
Sample 4	0.41gm	
Sample 5	0.40gm	
Sample 6	0.41gm	
Sample 7	0.41gm	
Sample 8	0.40gm	
Total weight = 3.24/8 = 0.405gm		

13.2 Thickness test:

Thickness test is carried out by using a Digital Vernier caliper. For measurement of Uniformity of thickness5 films are randomly selected and thickness is measured at five locations (centre and four corners), and the mean thickness is calculated Samples with air bubbles, nicks or tears and having mean thickness variation of greater than 5% are excluded from analysis.

Fig 11: Thickness test for ADB Buccal Films

The thickness of the films prepared with HPMC polymer combination ratios was found to be in the range of 0.12-0.14 mm & the average is .138mm in central region. So that it is suggesting that the films were thin enough and they would not cause any inconvenience after their application to the buccal cavity

13.3 Surface pH Determination:

Surface pH measured by the dissolving one oral film in 10ml distilled water. The resulting solution is then placed under digital pH meter to determine the surface pH. The surface pH of oral strip is calculated in order to examine the risk of any adverse effect in vivo. Since acidic or alkaline pH may cause irritation in the oral mucosa, it is determine to maintain the surface pH as close to neutral as possible. The pH range of 6-7 is considered acceptable. The process is repeated for three films and means pH was calculated. Which is about,

Surface pH **ADB** Buccal Films =7.1+6.9+6.8/3

S.No.	Formulation No. of Films	Disintegration Time (In Seconds)
1.	F1	52 Sec
2.	F2	58 Sec
3.	F3	77 Sec
4.	F4	90 Sec
5.	F5	58 Sec
6.	F6	45 Sec
7.	F7	55 Sec
8.	F8	58 Sec

Fig 12: Determination of Surface pH of ADB Buccal Films

13.4 Stability Study:

Stability test at Room Temperature (33º C):- Stable

Stability test at Cold Temperature (4º C):- Stable but get dissolve if contact with moisture.

Stability test at High Temperature (45º C): - Unstable get melt

13.5 Disintegration test:

Disintegrating time is defined as the time (second) at which a film breaks when brought into the contact with water or saliva. The disintegration time is the time when a film starts to break or disintegrate. Thickness and mass play a role in determining the dissolvable films physical properties. Disintegration test is done by Petridish Method.

13.5.1 Petridish Method: In this method 2 mL of distilled water was placed in a petridish and one film was added on the surface of the water and the time required until the oral film dissolved completely was measured. Drug-loaded films were investigated under both methods. The estimations were carried out in triplicate.

Table No.7 Reading of Disintegration Time of ADB Buccal Films by Petridish Method

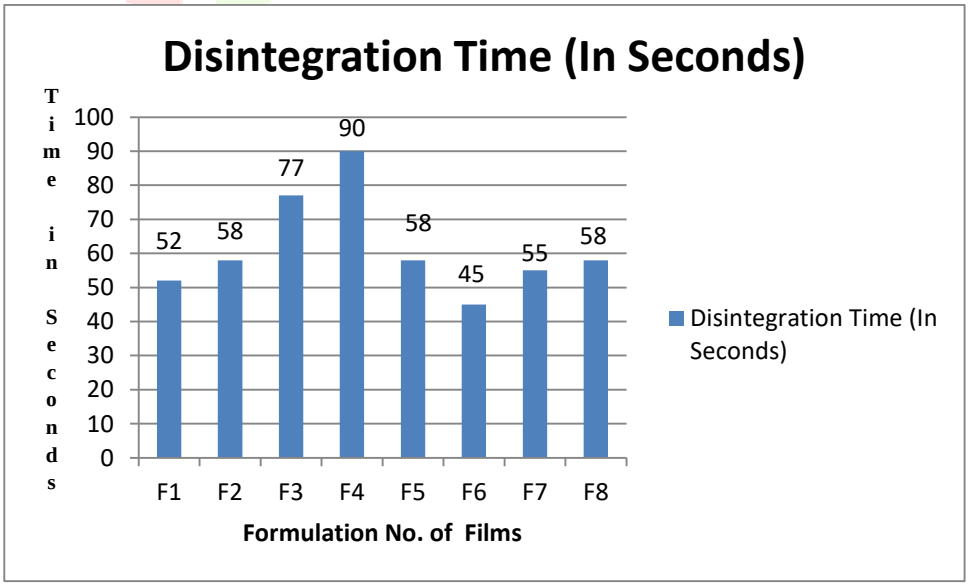

Fig 13: Disintegrating time of various formulations of ADB Films

13.6 Dissolution test:

Dissolution is defined as the amount of drug substance that goes into the solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent concentration. In vitro release studies are carried out in modified USP XXIII apparatus (paddle over disk). The in vitro dissolution studies were conducted using 500 mL of artificial saliva as dissolution medium with modified type 5 dissolution apparatus. A temperature of 37°C and 50 rpm was used. Each film with a dimension of appropriate size equivalent to 5 mg of Amlodipine was placed into a dissolution flask. Five mL samples were withdrawn at 1, 2, 3, 4, 5, 6, 7.8,9 &10 minute time intervals and every time replaced with 5 mL of fresh dissolution medium. The samples were analysed by measuring absorbance at 238 nm. The dissolution experiments were conducted in triplicate.

$$\textbf{\% Drug release per film} = \frac{\text{Sample Absorption}}{\text{Standard Absorption}} \times \frac{\text{Standard Dilution}}{\text{Sample Dilution}} \times 100\% \quad \ldots\ldots 7.1$$

13.7 Uniformity of drug content/Percentage of drug content:

This parameter can be determined by dissolving known weight of film by homogenization in 100 ml of stimulated saliva/ water of pH 6.8 for 30 min with continuous shaking.

Table No.8: % Drug of release per film at different time intervals

S.No.	Formulation No. of Films	Drug Release Time at different time intervals (in minutes)	% Drug release per film
1.	F1	At 1 minute	3.44%
2.	F2	At 2 minute	37.03%
3.	F3	At 3 minute	37.50%
4.	F4	At 4 minute	57.57%
5.	F5	At 5 minute	60.4%
6.	F6	At 6 minute	59.09%
7.	F7	At 7 minute	62.31%
8.	F8	At 8 minute	75.01%
9.	F9	At 9 minute	77.77%
10.	F10	At 10 minute	80.89%

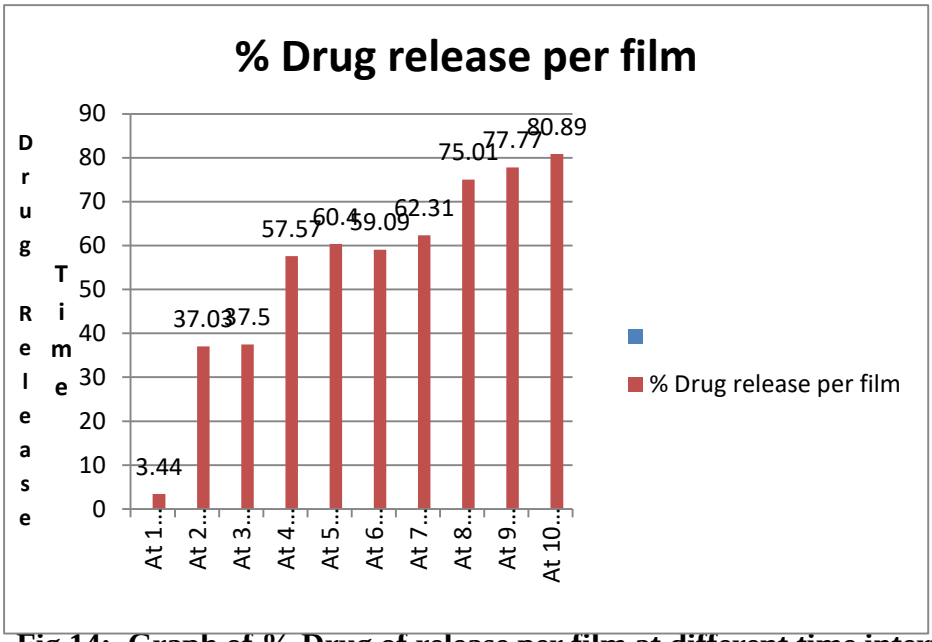

Fig 14: Graph of % Drug of release per film at different time intervals

Result & Discussion

Finally the Amlodipine buccal films are prepared by solvent casting method by using the composition mentioned in Table no. 6.1 & evaluation is also done .The prepared buccal films have citric acid taste along with peppermint odour. It is passed all the evaluation tests. The drug already pass all preformulation test like Organoleptic properties / Physical appearance test, Melting point , Solubility and flow properties of the powder drug etc. The formulation pass all the essential tests like Calculation of drug loaded in the film, Weight variation test, Thickness test, Surface pH Determination, Stability Study, Uniformity of drug content, Disintegration test, Dissolution test:& Physical appearance of prepared films

Conclusion

Hence, Amlodipine Besylaate buccal films were prepared by following the solvent casting method is one of the best methods for the formulation of buccal films. The above mention composition is one of the best compositions for the formulation of Amlodipine buccal films. Fast dissolving buccal films have gained popularity because of better patient compliance, rapid drug delivery system, drug is directly absorbed into systemic circulation, first pass metabolism and degradation in gastrointestinal tract can be avoided. Fast dissolving buccal films can be a better option to optimize therapeutic efficacy of various active pharmaceutical ingredients in the future.

Recommendations

- Since the drug is highly moisture sensitive, its stability to moisture should be studied.

- Since the drug is very bitter, addition of only sweetening agent would not be sufficient for taste masking. Other methods of taste masking should be crucial factors, the effect of plasticizer and surfactant concentration can also be studied to obtain even more optimized formulation with better results.

- Other methods of preparation like Semisolid/Hot melt extrusion/Solid dispersion extrusion or Rolling method can also be used since preparation method also lead to variation of test results.

- Tensile strength of the formulation has not been included in the study but is important parameter as this paly vital role for processing and shipment of the dosage form.

• Decreasing the concentration of HPMC increased the drug release rate. This indicates that HPMC concentration plays vital role in drug release rate.

REFERENCES

1. Duyen, Huynh Thi My, Dao Long Chau, Vo Dao Thao Vy, Tran Cao Truc Linh, and Pham Nguyen Quoc Thong. "Research on the preparation of amlodipine 5mg immediate-release film-coated tablets to improve active ingredient's stability." tạp chí y dược học cần thơ 5 (2023): 112-120.

2. Liu, Jie, Yongguo Zhang, Hui Li, Chao Liu, Peng Quan, and Liang Fang. "The role of hydrophilic/hydrophobic group ratio of polyvinyl alcohol on the miscibility of amlodipine in orodispersible films: From molecular mechanism study to product attributes." International Journal of Pharmaceutics 630 (2023): 122383.

3. Kumar, Prateek, and Rajneesh Kumar Gupta. "Formulation and Characterization of Mouth Dissolving Films of Amlodipine using Natural Polymer." Research Journal of Pharmacy and Technology 15, no. 8 (2022): 3651-3655.

4. Sha, A., and S. Pravin. "Formulation and evaluation of mouth dissolving films of amlodipine besylate by using natural and synthetic polymers." Research Journal of Pharmacy and Technology 15, no. 11 (2022): 5154-5157.

5. Sumaiyah, Sumaiyah, Julia Mentari, and Suryanto Suryanto. "The effect of crospovidone on the dissolution profile of amlodipine besylate from fast orally dissolving film." Open Access Macedonian Journal of Medical Sciences 7, no. 22 (2019): 3811.

6. Bernard, Shyni, Molly Mathew, and K. L. Senthilkumar. "Spectrophotometric method of estimation of Amlodipine besylate using hydrotropic solubilization." Journal of Applied Pharmaceutical Science Issue (2021): 177-180.

7. Shinde P, Salunkhe V, Magdum C.Buccal film:an innovative dosage form designed to improve patient compliance. Int. J of Pharmaceutical and Chemical science,2012; 1(4):1262-1278

8. Nair AB, Kumaria R, Harsha S. In vitro techniques to evaluate buccal films. J of Controlled Release. 2013;166:10-21

9. Shojaei AH. Buccal mucosa as a route systemic drug delivery: a review. Journal of Pharmaceutical science.1998;1(1):15-30

10. Bhati R, Nagranjan R.A Detailed review on oral mucosal drug delivery system. Int J of pharmaceutical science and research.2012;3(1):659-681

11. Singh SP, Singh RP, Gupta SK. Buccal mucosa as route for drug delivery: mechanism, design and evaluation.Research J of Pharmaceutical, biological and chemical sciences.2011;2(3):358-372

12. Mishra S, Kumar G,Kothiyal P. A review article: Recent advances in buccal patches.2012;1(7):78-86.www.thepharmajournal.com

13. Tangri P,Sateesh Madhav NV.Oral mucoadhesive drug delivery system. Int J of biopharmaceutics 2011;2(1):36-46

14. Patricia DV, Maria AN, Antonio AS, Saliva composition and function: a comprehensive review. Journal of Contemporary of dental practice.2008;9(3):1-11

15. Sharma N, Jain S, Satish S.Buccoadhesive drug delivery system: a review.J of Adv.Pharm.Edu and Reserch.2013;3(1);1-15

16. Akhter H. A comprehensive review on buccal drug delivery. Int. J of Pharmaceutical Research and development.2011;3(1):59-77

17. Tayal S, Jain N.Buccal conrol drug delivery system:a review. International journal of Pharmaceutical science and research. 2011;2(1):13-24

18. Ragvendra NG, Shravani B, Reddy MS.Overview on buccal drug delivery systems.Journal of pharmaceutical science and research.2013;5(4):80-88

19. Parmar HG, Jain JJ, Patel TK. Buccal patch: a technical note. Int. J of Pharmaceutical Sciences review and research.2010;4(3):178-182

20. Radha MB, Murthy VS. Buccal film drug delivery system-an innovative and emerging Technology. Molecular Pharmaceutics and Organic Process Research. 2013; 1(3):1-6

21. Arunachalam A, Karthikeyan M, Konam K. Fast dissolving drug delivery: a review. J of global trend in pharmaceutical science.2010;1(1):92-110

22. Mundhe B, Kadam V, Jadhv S. A short review on fast dissolving oral film.Wprld J of Pharmacy and pharmaceutical sciences. 2014;3(3):463-475

23. Neelagiri R, Reddy MS, Rao NG. Buccal Patch as Drug delivery system: an overview. International Journal of Current Pharmaceutical Research.2013;5(2):42-47

24. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral film: an innovative drug delivery and dosage form.Int J of Chemtech Research.2010;2(1):576-583

25. Nagich U, Choudhary V. Formulaion and Development of Metoprolol Tartarate bucco adhesive films. The Pharma Research. 2009;(1):41-53

26. Lohani A, Prasad N, Arya R. Formulation and characterization of mucoadhesive buccal film of Ranitidine Hydrochloride.2011:2(9):2457-2462

27. Mahajan A, Chhabra N, Aggarwal G. Formulation and characterization of fast dissolving buccal film. Scholars Research Library.2011;3(1):152-165

28. Kaur A, Kaur G. Mucoadhesive buccal patches of interpolymer complexes of chitosan pectin for delivery of carvedilol. Saudi Pharmaceutical Journal. 2012;(20):21-27

29. Verma N, Ghosh AK, Chattopadhyay P. Preparation and in vitro assessment of mucoadhesive buccal patches containing Carvedilol. Int. J of Phrmacy and Pharmaceutical Sciences.2011;3(3):218-220

30. Desu P, Sahu M. Formulation and evaluation of fast dissolvinfg film of zolmitriptan. International Research J of Pharmacy. (2012);3(1):373-376

31. Shridhar I, Joshi A. Formulation and characterization of buccal patch of Ondanserton hydrochloride. Int. J of Pharmaceutical Research and development.2013:5(8):84-94

32. Perioli L, Ambrogi V. Development of mucoadhesive patches for buccal administration of Ibuprofen. J of Controlled release. 2004;99:73-84

33. Costa P, Lobo J. Modeling and comparison of dissolution profiles. European J of Pharmaceutical sciences. 2001;(13):123-133

34. Govindsamy P, Keasavan BR. Formulational unidirectional release of buccal patch of carbamazepine and study of permeation through of porcine buccal mucosa. Asian Pacific J of tropical biomedicine. 2013;3(12):995-1002

35. John AS, Goli D. Development and evaluation buccoadhesive drug delivery system of Atovavastin calcium. J of Current Pharmaceutical Research. 2010;1:31-38

36. Kshirsagar N, Thamada N. Design and evaluation of chitosan containing muccoadhesive buccal patch of Fluoxtine HCL. 2012;2(6):1-5

37. Charyulu RN, Shripriya BS. Design and characterization mucoadhesive buccal patch containing antifungal agent for oral candidiasis. Int J of Pharmaceutical and Phytopharmacological Research. 2012:1-12

38. Bhyan B, Jangra S. Formulation and Evaluation of fast dissolving sublingual film of Rizatriptan Benzoate. Int J of Drug Development and Research. (2012);4(1):133-144

39. Murthy VS. Buccal film drug delivery system- an innovative and emerging technology. Journal of Molecular pharmaceutics and organic process research. 2013; 1(3).

40. www.pharamaexcipients.comHow to cite this article: Jagtap VD. Buccal film a review on novel drug delivery system. International Journal of Research and Review. 2020; 7(6): 17-28.

41. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving strips: A novel approach for the delivery of verapamil, Int.J. ChemTech Res, 2010, 2(1).

42. Kerins DM, Robertson RM, Robertson D. Chapter 32. Drugs and the drugs used for the treatment of myocardial ischemia. Goodman & Gilman's the Pharmacological Basis of Therapeutics. 10th Ed. JG Hardman, LE Limbird, AG. Gilman, eds. McGraw-Hill, New York, 2001; 843-63.

43. Available at http://www.rxlist.com/norvasc- drug.html.

44. Available at http://www.drugs.com/pdr/amlodipine-besylate.html.

45. Rowe RC, Sheskey PJ, Owen SC, Sodium starch glycolate, Pharmaceutical Excipients, Pharmaceutical Press and the American Pharmacists Association.

46. Rowe RC, Sheskey PJ, Owen SC, Glycerine, Pharmaceutical Excipients, Pharmaceutical Press and the American Pharcists Association.

47. Shimoda H, Taniguchi K, Nishimura M, Matsuura K, Tsukioka T, Yamashita H et al. . Preparation of a fast dissolving oral thin film containing dexamethasone, European Journal of Pharmaceutics and Biopharmaceutics, 2009, 73, 361–365.

48. Patel R, Shardul N, Patel J, Baria A. Formulation, development & evaluation of oral fast dissolving anti-allergic film of levocetrizine dihydrochloride Arch Pharm Sci & Res, 2009, 1(2), 212 – 217.

49. Mahesh A, Shastri N, Sadanandam M. Development of taste masked fast disintegrating films of levocetirizine dihydrochloride for oral use. Curr Drug Deliv. 2010; 7:21–7.

50. Patel R, Naik S, Patel J, Baria A. Formulation development and evaluation of mouth melting film of ondansetron. Arch Pharm Sci Res. 2009; 1:212–7.

51. Mohammed A, Harish N, Charyulu R, Prabhu P. Formulation of chitosan-based ciprofloxacin and diclofenac film for periodontitis therapy. Trop J Pharm Res. 2009; 8:33–41.

52. Siewert M, Dressman J, Brown CK, Shah VP. FIP; AAPS. FIP/AAPS guidelines for dissolution/in vitrorelease testing of novel/special dosage forms. AAPS PharmSciTech. 2003; 4:E7.

53. M Slowson; S Slowson. Pharm Times, 1985, 51, 90-96.

54. KD Tripathi. In Essentials of Medical Pharmacology, 6th ed, JP Medical Publishers, 2003, p. 606-607.

55. Drug Delivery via Dissolving Strips, Drug Discovery & Development, 2007, 10 (7), 10. Available from URL: http//en.wikipedia.org/wiki/thinfilmdrugdilvery.

56. R Dixit; S Puthli. J of Controlled Release: (Mumbai, India) Official J of Controlled Release Society, 139(2), 94-107.

57. R Patel; N Shardul; J Patel; A Baria. Arch Pharm Sci & Res, 2009, 1 (2), 212-217.

58. Sumitha CH; Karunasree N; Divya B; Madhavi K; Vimal Kumar VM; Charbu NN. Int.Chemical Research, 2009, 1(2), 24-27.

59. LH Reddy; B Ghose; Rajneesh. Indian J.Pharma. Sci, 2002, 64(4), 331-336.

60.Kuchekar; BS; V Arumugam. Indian J. Pharm. Edu, 2001, 35, 150.

61. S Bhaskaran; GV Narmada. Indian Pharmacist, 2002, 1(2), 9-12.

62. NH Indurwade; TH Rajyaguru; PD Nakhat. Indian Drugs, 2002, 39(8), 405-09.

63. PV Devrajan; SP Gore. Express Pharma Pulse, 2000, Nov. 23, 7(1), 16.

64. AS Kulkarni; HA Deokule; MS Mane; DM Ghadge. J current Pharm. Research, 2010, 2 (1), 33-35.

65. P Sakellariou; RC Rowe. Prog. Polym. Sci, 1995, 20, 889 -942.

66. GS Banker. J. Pharm. Sci, Jan 1966, 55, 81-88.

67. LME McIndoe; RC Rowe; PJ Sheskey; SC Owen. In Handbook of Pharmaceutical

Excipients, Pharmaceutical press, London, 2006, p. 128 - 130.

68. A Wale; PJ Weller. In Handbook of Pharmaceutical Excipients, 2nd edition, 1994, p. 24, 27, 352,448.

69. Prakash; GE DuBois; JF Clos; KL Wilkens; LE Fosdick. Food Chem. Toxicol, 2008, 46, 75 - 82.

70. AH Chapdelaine; DJ Zyck; MR Dzija. US Patent 6740332, 2004.

71. SD Barnhart; MS Slaboda; Drug Dev. Tech, 2007, 1, 34-35.

72. M. Repka; J Swarbrick; J Boylan. In Encyclopedia of Pharmaceutical Technology, 2nd Edition, 2002, vol 2, p. 1488–1504.

73. F Cilureo; I Cupone; P Minghtti; F Selmin; L Montanari. J Pharma Biopharma 2008, 17Vol.

74. RC Mashru; VB Sutariya; MG Sankalia; PP Parith. Drug Dev. Ind. Pharm, 2005, 1, 25-34.

75. S Malke; S Shidhaya; J Desai; V Kadam. Internal J. of Pediatrics & Neonatology, 2010, 2 Vol.

76. Yelave, Adesh, Geeta Sameer Bhagwat, and Adnan Rehmatullah Siddique. "Incorporation of Antihypertensive Class IV Drug in Novel Buccal Film Formulation." *Asian Journal of Pharmaceutical Research* 14, no. 1 (2024): 15-24.

77.Panda B, Dey N, Rao M. Development of innovative orally fast disintegrating film dosage forms: a review. Int J Pharm Sci Nanotech, 2024; 5(2): 1666-74.

78. Patil PC, Shrivastava S, Vaidehi S, Ashwini P. Oral Fast Dissolving drug delivery system: A modern approach for patient compliance. Int J Drug Regulatory Affairs, 2024; 2(2): 49-60.

79. Patel AR, Prajapati DS, Raval JA. Fast dissolving films (FDFs) as a newer venture in fast dissolving dosage forms. International journal of drug development and research, 2024; 2(2): 232-46.

80. Nagar P, Chauhan I, Yasir M. Insights into polymers: film formers in mouth dissolving films. Drug Invention Today, 2024; 3(12): 280-9.