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Formulation and in Vitro Evaluation of Fast Dissolving Film of Deflazcort

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ABSTRACT

The present research is particularly based on increasing safety and efficacy of active drug molecule through novel system of oral drug delivery. Deflazacort is a synthetic steroidal drug which was having anti inflammatory effect and to decrease inflammation in various different diseases conditions. Deflazacort acts within cells to prevent the release of certain chemicals that are requried in the immune system. These substances are generally involved in production in immune and allergic responses; resulting in inflammation. By declining the release of chemical substances in the particular area, inflammation can be decreased.. Severe allergic reactions, inflammation of the joints in arthritis and inflammation of the lungs in asthma can be reduced by using the drug. Deflazacort reduces the numbers of white blood cells. And in Nephritic Syndrome, patients are required to take this drug for long times. Fast dissolving films of Deflazacort were by solvent casting method.Propylene glycol which was used as Plasticizers which was able to impact flexibility and folding endurance to the films. The optimized formulation (F8) was shown better formulation, good folding endurance, and better dissolving property within 2 minutes. The optimized formulation F8 was chosen and their optimum results were found to be in close agreement with experimental finding.

Key words: Fast dissolving film, Deflazcort, hydroxypropyl methylcellulose, polyvinyl alcohol, solvent casting,

INTRODUCTION

Oral route is the most favourable route by medical practitioners and manufacturer for its highest adequacy of patients. This route is the most acceptable for the patients due to the ease of consumption and the avoidance of pain. About 60% dosage forms are available in oral solid dosage form. Fast dissolving drug delivery systems were first developed in 1970 was an alternative of tablets and capsules. Each pharmaceutical companies wants to formulate the novel drug delivery systems which has higher bioavailability, quick action and the most patient complance. Many patients especially geriatric and paediatrics and many other patients like mentally disabled uncooperative patients have difficulties to swallow the tablets and capsules. So, fast dissolving drug delivery system has started gaining popularity and acceptance among these patients with fear of choking. Patient convenience and compliance oriented research has resulted in bringing out safer and newer drug delivery system has acquiring popularity and increases customer's choice for the reason of rapid disintegration, dissolution, self administration even without water and chewing.[1]

Deflazacort is a corticosteroidal drug ,oxazoline derivative of prednisolone, characterized by a high binding affinity glucocorticoid receptors to tissue which elicit anti-inflammatory and immunosuppressive effects. Deflazacort considerably inhibits the propagation of mononuclear cells derived from human peripheral blood, and inflammatory cytokines release by these cells. Thus deflazacort is most effective in symptoms and objective indices of disease activity in rheumatoid arthritis 2. RA is a chronic disorder in which, the body's own immune system starts to attack body tissues, reasons of which are unknown. This disorder is accompanied with swelling, stiffness and pain. In this disorder the attack is not only directed at the joint but to many other parts of the body. In RA, the joint lining and cartilage gets more damaged which eventually results in erosion of two opposing bones. Based on the studies, it has been reported that deflazacort could be used in treatment of RA. It is as efficacious as prednisolone with less adverse effects as compared to other corticosteroids3.

Material and methods

Materials

The following materials of Pharma grade were used as supplied by the manufacturer.

Deflazacort was received as gift sample from Macleods Pharmaceuticals Limited ,HPMC from Accent microcell industries ,PEG400 from Spectrum Pharmaceuticals, Ethanol from Symods pvt ltd.

Methods [5]

Preparation Of Calibration Curve In Methanol

Accurately weighed 10 mg of deflazacort was taken in a volumetric flask, dissolved in small amount of methanol, and finally diluted with methanol to get a stock solution of 100 µg/ml .Stock solution was further diluted with methanol to obtain different concentrations (1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30 µg.ml Confirmation of λmax was done by scanning suitable dilutions of the stock against the same solvent system. [36] Preformulation studies focus on those physicochemical properties of new drug substances, development of an efficacious dosage form. In simple terms preformulation investigations merely confirm that there are no significant barriers to the compound's development.

Deflazacort was subjected to various preformulation test such as identification tests and drug polymer interaction studies.

Organoleptic Properties:- Pure drug samples was observed for colour, taste,and odour.

Solubility :- Solubility is expressed in terms of parts per million of solvent in which 1g of solid is soluble. Solubility of the powder in different solvents like water , ethanol etc was determined .

Melting Point :- The melting point was carried out by using capillary tube method.

Formulation development of Deflazacort

Table:- 1 composition of formulation batches of Fast dissolving Films

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
HPMC(mg)	100	-	200	-	**150**	-	**200**	**400**
PVA(mg)	-	**100**	-	**200**	-	**250**	-	-
Propylene Glycol(ml)	**0.3**	**0.4**	**0.5**	**0.3**	**0.5**	**0.5**	**0.6**	**0.4**
Ethanol(ml)	**20**		**30**	**10**	-	-	**10**	**20**

Preparation of placebo film for Deflazacort

To prepare placebo film, a proper selection of film former and plasticizer is required. In this research work, various film formers like- HPMC , PVA, , plasticizers like- Propylene glycol, PEG-400, glycerol and tween 80 were used. Film were prepared by solvent casting method and dried in hot air own at 50 °C.

Selection of film former

Selection of the film former was done by preparing placebo films of film former like: HPMC ,PVA. Films were prepared by using solvent casting method.

Selection of cellulose derivatives

Initially cellulose derivatives like HPMC (15 cps), HPC are employed in different concentration

Selection of plasticizers for cellulose derivatives

Various plasticizers like propylene glycol, polyethylene glycol - 400, glycerol and tween 80 were used. Their concentrations were varying from 5-15 % w/w of plasticizer concentration.

Preparation of FDFs of Deflazacort

All the selected film formers and modifiers were soaked in half the quantity of water separately for 8 hours to get uniform dispersion and mixed both the solution with stirring. Deflazacort was dissolved in a portion of water. This solution was added to polymeric solution and mixed well to obtain homogenous solution followed by addition of plasticizer/s, neotam and citric acid. The solution was mixed well to get uniform dispersion. Solution was then casted into petridishes having surface area of 64 cm2 and 1.3 cm wall height. Petridishes were kept in hot air oven for 8 hours at 50˚ C. After drying films were removed with the help of sharp blade and kept in desicator for 24 hrs before cutting into small pieces having area of 6 cm2 for each film. Films with air bubbles, cuts or imperfections were excluded from further study. Selected films were subjected for different evaluation parameters.

Evaluation parameters

Appearance

All prepared films were checked for their appearances either they are transparent or opaque.

Weight variation and thickness

Films were evaluated for its weight variation and thickness. Weight variation was evaluated by using electronic balance and thickness was measured using Digital Vernier Calipers.

Mechanical properties [6]

Various mechanical properties like tensile strength, % elongation, elastic modulus and folding endurance were evaluated for prepared films.

Folding endurance [7]

A film of 6 cm2 was repeatedly folded and unfolded at the same place till it breaks. The number of times, the film could be folded at same place, without breaking was recorded as the value of folding endurance. This gives an indication of brittleness of the film.

Surface pH

The surface pH of rapid dissolving films was determined in order to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH as close to neutral as possible . The films were allowed to swell in closed petridish at room temperature for 30 minutes in 1ml of distilled water. Solution was placed under digital pH meter to determine the surface pH.

Content uniformity [8]

The drug content of optimized films were assayed by random sampling of the 5 films of 6 cm2 from one petridish (64 cm2), each film was dissolved in 50 ml volumetric flask containing water. Solution was subjected to centrifugation for 15 min at 2500 rpm. The supernatant liquid was diluted to obtain 10 µg/ml solution and passed through Whatman filter paper. Filtered solution was analyzed by double beam UV Spectrophotometer at 210 nm against 6.4 pH phosphate buffer solution as blank .

In-vitro disintegration time

Disintegration time provides an indication about the disintegration characteristics and dissolution characteristics of the film. The require size of film (6 cm2) of selected formulations was placed in a glass petridish (9 cm diameter and 1.3 cm wall height) containing 10 ml of distilled water and left undisturbed. The time was noted down till film was completely converted into small pieces. Test was performed 3 times on each formulation.

***In-vitro* dissolution studies** [9]

An in-vitro dissolution study was performed for the films of selected formulations for 3 minutes in USP paddle apparatus using pH 6.4 phosphate buffer solution. Dissolution medium was kept at 37° C ± 2 ºC and rotated at 500 rpm. The samples (5 ml) were withdrawn after every 30 sec and replaced with fresh buffer (pH 6.4) solution. One ml sample was then taken and diluted up to 10 ml in volumetric flask. The samples were analyzed for the drug content using UV spectrophotometer at 210 nm. Dissolution was performed 3 times for each formulation to calculate drug release.

RESULTS AND DISCUSSION

Preformulation studies [9]

Specification:- White crystalline powder, odourless.

Solubility:- Solubilty is expressed as in terms of parts per million of solvent in which 1g of solid is soluble.Solubility of the Deflazacort in different solvents like water, ethanol etc was determined at 20^0 c . Deflazacort is springly soluble in Ethanol, Methanol and in Acetone and very slightly soluble in water.

Melting Point:- Melting point is carried out by using Capillary tube method.

CALIBRATION CURVE OF DEFLAZCORT

Table -2 calibration curve of Deflazcort

Concentration (µg/ml)	Absorbance
2	0.107
6	0.293
10	0.463
14	0.593
18	0.763

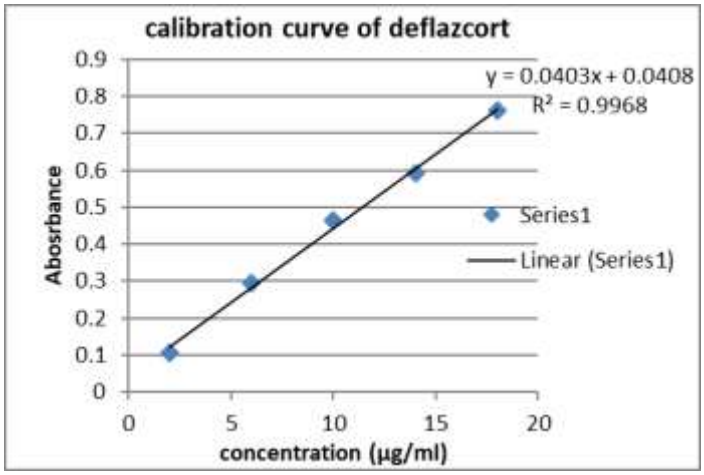

Figure -1 Calibration curve of deflazcort

EVALUATION PARAMETER

Thickness:-

A micrometer screw gauge was used to measure the film thickness. In order to obtain uniformity of film, thickness is measured at 5 different locations. The thickness of the film should be less than 5 %. The thickness of fast dissolving films of all formulations given in table 3

Table -3 Thickness of fast dissolving films

Formulation	Thickness
F1	0.58
F2	0.55
F3	0.59
F4	0.51
F5	0.53
F6	0.52
F7	0.55
F8	0.57

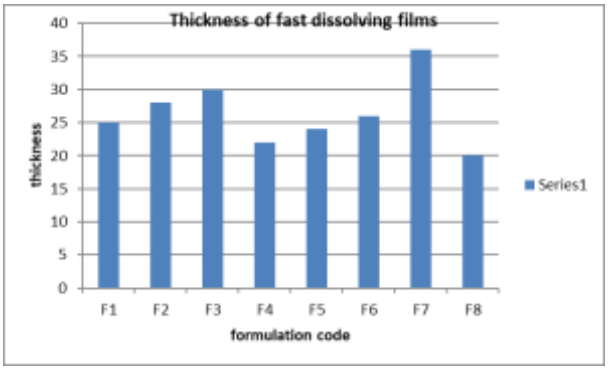

Figure -2 Thickness of fast dissolving films

Folding Endurance :-

To determine folding endurance, a film is cut and rapidly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of folding endurance.The folding endurance of fast dissolving films of all formulations given in table -4.

Table-4 Folding endurance of fast dissolving films

Formulation	Folding Endurance
F1	9
F2	10

F3	11
F4	13
F5	8
F6	6
F7	9
F8	12

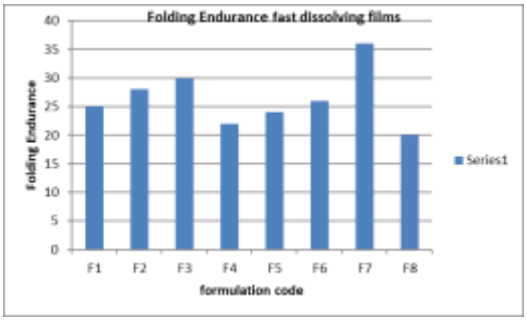

Figure -3 Folding endurance of fast dissolving films

Percentage elongation-

It was calculated by Percentage elongation = Increase in length of strip × 100 Initial length of strip . The percentage elongation of fast dissolving films of all form ulations given in table 5.

Table-5 % elongation of fast dissolving films

Formulation	% elongation
F1	8
F2	11
F3	9
F4	10
F5	12
F6	11
F7	9
F8	8

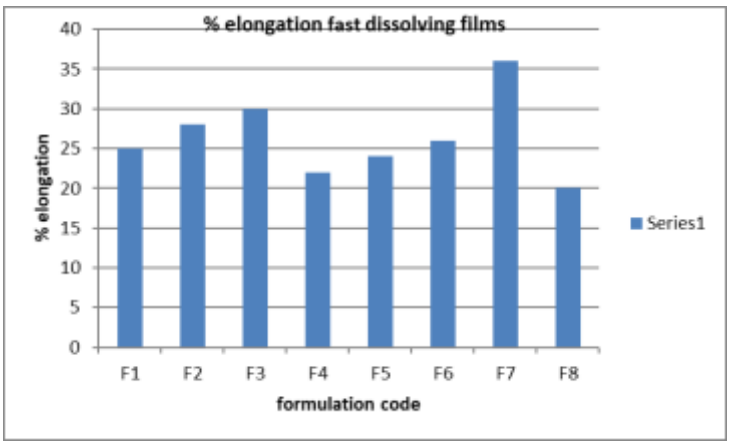

Figure -4 % elongation of fast dissolving films

In vitro disintegration time

In-vitro disintegration Petri dish method 2 ml of distilled water was placed in the petri dish and one film was added on the surface of water and the time measured until the oral film was dissolved completely.

Table-6 In vitro disintegration time of fast dissolving films

Formulation	In vitro disintegration time(sec)
F1	25

F2	28
F3	30
F4	22
F5	24
F6	26
F7	36
F8	32

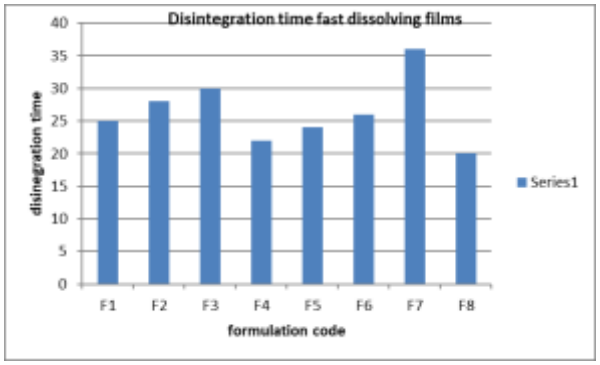

Figure -4 In vitro disintegration time of fast dissolving films

Weight Variation:- Ten films were randomly selected and their average weight was weighed. Individual films were weighed and compared with the average weight for the deviation. The weight variation of fast dissolving films of all formulations given in table 7

Table-7 Weight Variation of fast dissolving films

Formulation	Weight Variation
F1	54
F2	55
F3	55
F4	51
F5	53
F6	52
F7	53
F8	57

CONCLUSION

The primary objective of this work was to develop a mouth dissolving film with Deflazacort, along with basic ingredients like polymers, Plasticizers, sweeteners, saliva stimulating agents, and flavouring agent. The films were prepared by solvent casting method. The Plasticizers Propylene glycol which was able to impact flexibility and foldind endurance to the films . The optimized formulation (F8) was shown better formulation, good folding endurance, better dissolving property within 2 minutes . Therefore rapid drug release was achieved for immediate onset of action which is beneficial when compared to conventional films dosage form

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