INVITRO EVALUATION OF TRIAMCINOLONE BUCCAL TABLETS - A STUDY

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ABSTARCT

Regulated drug release in "first order manner attained in the current study indicates that the hydrophilic matrix tablets" of-Triamcinolone was prepared using HPMC K4M, HPMC K100M and HPMC K15M "can successfully be employed as a buccoadhesive controlled released during delivery system." Slow, controlled and complete release of-Triamcinolone over a period of-12 hours was obtained from matrix tablets formulated employing HPMC K4M (TR2 Formulation) with 98.56 % drug release.

***Keywords**: Buccal tablet, Triamcinolone, HPMC K4M, HPMC K100M, HPMC K15M.*

INTRODUCTION

Buccal delivery, which is drug administration through the mucosal membranes lining the cheeks (buccal mucosa),

Advantages

- Significant reduction in dose related side effects.
- It provides direct entry of-drug into systemic circulation.
- Drug degradation in harsh gastrointestinal environment can be circumvented by administering the drug via buccal route.
- Drug absorption can be terminated in case of-emergency.
- It offers passive system, which does not require activation.
- Rapid cellular recovery following local stress or damage.
- Ability to withstand environmental extremes like change in pH, temperature etc.
- Sustained drug delivery.
- The potential for delivery of-peptide molecules unsuitable for the oral route.

Limitations

- Once placed at the absorption site, the dosage form should not be disturbed.
- Eating and drinking are restricted.
- There is ever present possibility that the patient may swallow the formulation.
- Drug swallowed with saliva is lost.
- Drugs which are unstable at buccal pH and which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odor cannot be administered by this route.
- Over hydration may lead to formation of "slippery surface and structural integrity of" formulation may get disrupted.

Osteoarthritis (OA) is characterized by deterioration of-articular cartilage and extensive subchondral bone remodelling , as well as by inflammation within the synovial lining of-the osteoarthritic joint . During OA progression, synovial macrophages become activated and secrete many pro inflammatory cytokines and growth factors. These "cytokines and growth factors are" thought to detrimentally change the articular joint. First, activated synovial macrophages have been proposed to enhance transforming growth factor (TGF) β production. Due to TGF β, synoviocytes increase their production of-bone morphogenetic protein 2 (BMP2) and BMP4; as a consequence, osteophytes develop within the OA joint.

Second, it is thought that enhanced growth factor and cytokine production by activated macrophages facilitates cartilage extracellular matrix (ECM) degradation, contributes to synovial fibrosis and induces pain. The "latter is of-special interest" because pain management plays a pivotal role in clinical management of-OA. Pain management for patients with OA can be achieved through analgesia with agents such as paracetamol, nonsteroidal anti inflammatory drugs or intra articular injection of-corticosteroids. Intra articular injection with corticosteroids provides excellent results for OA related pain and is an advocated treatment for individuals with knee OA . More specifically, triamcinolone acetonide (TA) injections are even more effective than other corticosteroids in reducing pain. In 1985, Williams et al. reported that TA quite effectively protected against osteophyte development in a preclinical model of-OA. This finding suggests that TA somehow intervenes with synovial macrophage activation and might prevent subsequent TGF β– induced osteophyte development. More recently, in 2014, this finding was reproduced in a post traumatic model of OA using intra articular injections of dexamethasone . The authors of-that study also showed that corticosteroid therapy reduced cartilage destruction. It remains unclear through which mechanisms corticosteroids exert this positive effect on macrophages and other joint tissues within the joint during OA development. This effect might result from the marked influence of-corticosteroids on macrophage differentiation. Inactive macrophages are able to differentiate into different active subtypes. First, the classically activated (or M1) macrophages are activated through a cell mediated immune response. Interferon (IFN) γ, lipopolysaccharides and tumour necrosis factor (TNF) are especially well-known inducers of- M1 macrophages . Alternatively activated (M2) macrophages are related to humoral immunity tissue repair . Interleukin (IL) 4 is known to induce a wound healing, M2 activated macrophage whose activity is related to tissue repair . Interestingly, in response to corticosteroids, yet another activated macrophage subtype develops; these are known as regulatory macrophages . Regulatory macrophages are considered anti inflammatory and produce large amounts of IL10 . Intra particular-injection of-TA might polarize macrophage activation towards this specific form of-M2 phenotype with subsequent beneficial effects on osteophyte formation and cartilage degradation. Recently, we established an in vivo model of- severe OA that shows severe degradation of-particular cartilage, enhanced subchondral

bone sclerosis formation and pronounced osteophyte formation . Using folate receptor β (FRβ) targeted single photon emission tomography/computed tomography (SPECT/CT) to quantitatively measure macrophage activation, we also found abundant activation of-synovial macrophages within knee joints in this rat OA model. In this rat model of-severe OA, we investigated the in vivo effect of-intra particular TA injections on macrophage activation using FRβ targeted SPECT/CT. We hypothesized that intra particular treatment with TA reduces the amount of-macrophage activation and therefore diminishes osteophyte formation as described by Williams et al. . Furthermore, using longitudinally applied micro–computed tomography (μCT) for in vivo bone analysis and ex vivo equilibrium partitioning of-an ionic contrast agent using micro–computed tomography (EPIC μCT), we also analyzed whether intra particular TA injections might have a beneficial effect on OA related subchondral sclerosis and cartilage degradation as well. To explain our in vivo results, we performed several in vitro experiments. In these experiments, we characterized M1 and M2 differentiated macrophages by their cell surface receptor expression. We analyzed whether the addition of-TA could polarize macrophages towards a certain subtype and whether TA influences FRβ expression.

METHODOLOGY

The goals of-the preformulation study are:

- To establish the necessary physicochemical characteristics of-a new drug substance.
- To determine its kinetic release rate profile.
- To establish its compatibility with different excipients.

Hence, preformulation studies on the obtained sample of-drug include colour, taste, solubility analysis, melting point determination and compatibility studies and flow properties.

Estimation of Triamcinolone:

A) Determination of-max of Triamcinolone in phosphate buffer pH 6.8 solution:

B) Standard calibration curve of Triamcinolone in phosphate buffer pH 6.8 solution:

Drug – Excipient compatibility studies Fourier Transform Infrared (FTIR) spectroscopy:

Preformulation parameters

The "quality of-tablet, "once formulated by rule, is generally dictated by the quality of- physicochemical properties of-blends". "There are many formulations and process variables involved in mixing" and "all "these can affect the characteristics" of-blends produced. The various characteristics of-blends tested as per Pharmacopoeia.

Angle of-repose:" Bulk density:

Tapped density

Measures of-powder compressibility:

Method of-"Preparation of-mucoadhesive tablets:

Buccoadhesive Tablets: **Preparation: Direct compression method has been employed to prepare buccal tablets" of- Triamcinolone using HPMC K4M, HPMC K15M, And HPMC K100M as polymers.**

INGREDIENTS	TR1	TR2	TR3	TR4	TR5	TR6	TR7	TR8	TR9
Triamcinolone	4	4	4	4	4	4	4	4	4
HPMC K4M	4	8	12						
HPMC K15M				4	8	12			
HPMC K100M							4	8	12
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	3	3	3	3	3	3	3	3	3
MCC pH 102	QS	QS	QS	QS	QS	QS	QS	QS	QS
TOTAL	80	80	80	80	80	80	80	80	80

Characterization of buccal tablets of Triamcinolone:

Evaluation of Mucoadhesive buccal tablets of Triamcinolone:

1) Hardness test:

2) Thickness:

3) Friability test:

4) Uniformity of weight:

5) Uniformity of drug content:

6) Swelling Index:

7) *In vitro* drug release study:

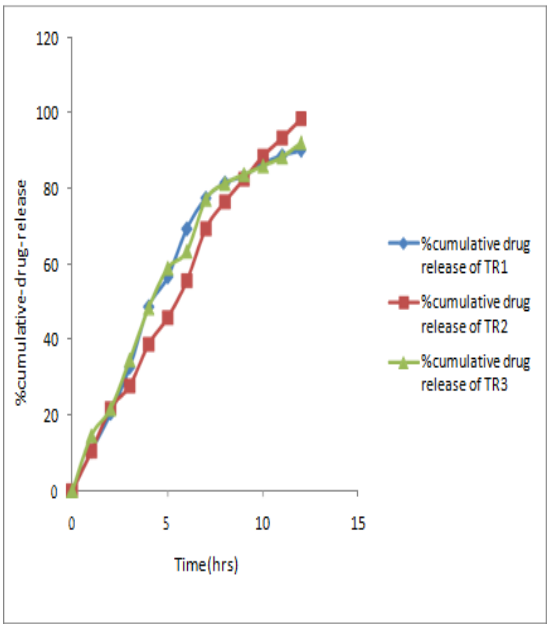
The study was carried "out in USP XXIII tablet dissolution test" apparatus" II "Labindia", "Mumbai", "India', "employing "paddle stirrer-at 50 rpm and 900 ml of-phosphate buffer" pH 6".8 "as dissolution medium maintained at" 37 0.5 0C. "The "tablet was supposed to release drug from one side only hence a one side of-tablet was fixed to glass disk with cyanoacrylate" adhesive". "The "disk was placed at the" bottom of-the dissolution vessel". "At "different time interval 5 ml of-sample was withdrawn and replaced" with fresh medium". "The samples were filtered through 0.25 □m-"membrane filter paper-and analyzed" for Triamcinolone "after appropriate dilution at 216 nm using Labindia, Mumbai, India UV Visible" spectrophotometer.

8) Release Kinetics

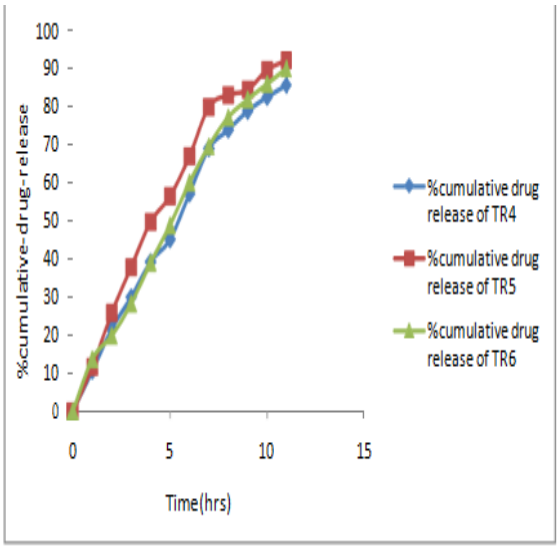
The mechanism of drug release from matrix systems was studied by using Higuchi equation, erosion equation and Peppas Korsemeyer equation.

RESULTS AND "DISCUSSION

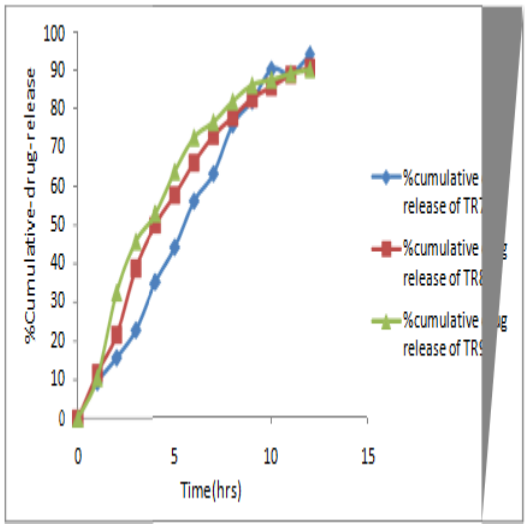
The main aim "of-this work was to" develop buccoadhesive tablets to release the drug at buccal mucosal site in unidirectional pattern for-extended period of-time without wash out of- drug by saliva". HPMC K4M, HPMC K15M, and HPMC K100M were selected as buccoadhesive polymers on the basis of-their matrix forming properties and mucoadhesiveness, while ethyl cellulose, being hydrophobic, used as a backing material.



Invitro dissolution graph of formulations TR1 TR3



"In vitro release data of Triamcinolone (TR7, TR8 & TR9)



"In Vitro dissolution graphs of" formulation (TR7, TR8 & TR9)

Application of "Release Rate Kinetics to "Dissolution Data":

"Various models were tested for explaining the kinetics of-drug release". "To analyze the mechanism of-the drug release rate kinetics of-the dosage form, the obtained data were fitted into zero order, first order, Higuchi, and Korsmeyer Peppas release model".

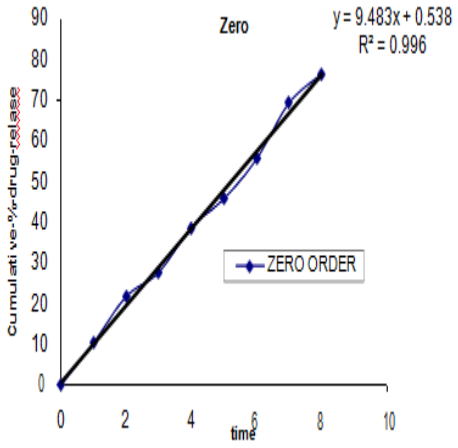


Figure: Zero order release kinetics graph:

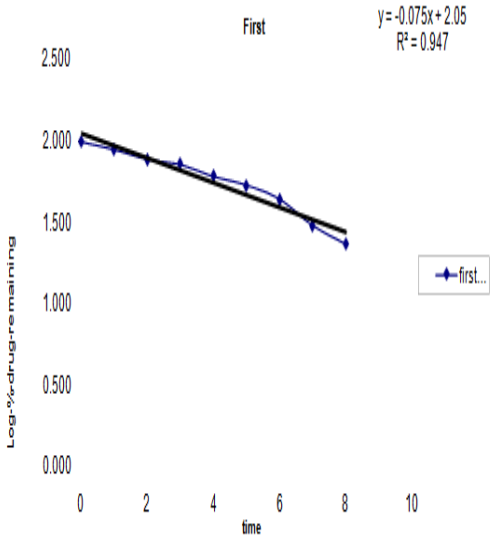


Figure - First order release kinetics graph

From the above results it is concluded that the drug release from the formulatedbucco adhesive tablets of Triamcinolone followed zero order kinetics and was diffusion controlled.

Figure - Ftir spectrum of pure drug

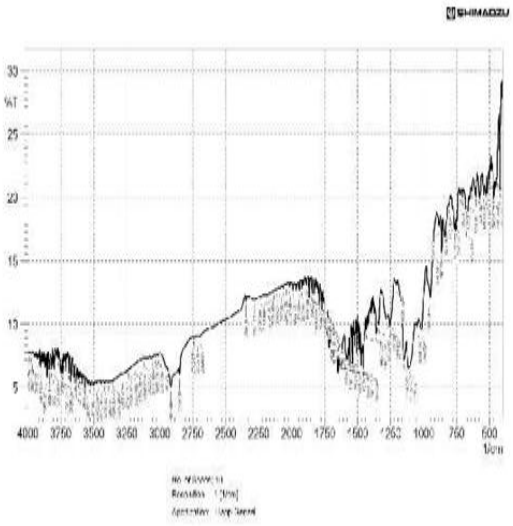


Figure - Ftir spectrum of optimized formulation

9. CONCLUSION

 "From the foregoing investigation "it may be conclude that the release rate of-drug from the buccal tablets can be governed by the polymer and concentration of-the polymer employed in the preparation" of-tablets".

 "Regulated drug release "in first order manner attained in the current study indicates that" the hydrophilic matrix tablets of-Triamcinolone was prepared using HPMC K100M and HPMC K15M can successfully "be employed as a buccoadhesive" controlled released during delivery system".

 "The pre compression blend foe" all formulations were subjected to" various evaluation parameters and the results were found to be within limits".

 "The post compression parameters for all the formulations also found to be within limits".

 Slow, controlled and complete release of-Triamcinolone over a period of-12 hours was obtained from matrix tablets formulated employing HPMC K4M (TR2

Formualtion) with 98.56 % drug release.

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