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Preparation of Mucoadhesive Patch Containing Tetracycline Hydrochloride For Treatment of Bacterial Infections

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ABSTRACT

The present study focuses on the formulation and evaluation of a mucoadhesive patch containing Tetracycline Hydrochloride for the effective treatment of localized bacterial infections, particularly in the oral cavity. Tetracycline Hydrochloride, a broad-spectrum antibiotic, was selected due to its potent activity against a wide range of gram-positive and gram-negative bacteria. The mucoadhesive patch was prepared using various combinations of polymers such as hydroxypropyl methylcellulose (HPMC), carbopol 934, and sodium carboxymethyl cellulose (NaCMC) through the solvent casting method. The formulated patches were evaluated for physicochemical parameters including thickness, weight variation, surface pH, drug content uniformity, folding endurance, swelling index, and mucoadhesive strength. In vitro drug release studies were conducted to determine the release kinetics, revealing a sustained and controlled drug release profile over several hours, making the system suitable for prolonged therapeutic action. Antibacterial efficacy was assessed using the agar diffusion method, which confirmed significant inhibition zones against common pathogens such as Staphylococcus aureus and Escherichia coli. The results suggest that the developed mucoadhesive patch is a promising localized drug delivery system, enhancing drug bioavailability at the site of infection, minimizing systemic side effects, and improving patient compliance.

KEYWORDS: Mucoadhesive patch, Tetracycline Hydrochloride, Local drug delivery, Oral infections, Bacterial infections, Bio adhesive polymers

INTRODUCTION

Among all the techniques of drug administration, oral administration is usually most preferred by both clinicians and patients. Similar: Still, oral administration of drugs has its disadvantages, such as hepatic first-pass metabolism and enzymatic degradation. The degradation in the gastrointestinal tract prohibits the oral administration of certain classes of

drugs. Thus, other. Absorptive mucosa is considered a potential site for drug delivery. Drug administration via the mucous membranes (e.g. nasally, orally, rectally).The nasal, rectal, vaginal, ocular, and oral cavity mucosal lining possesses specific benefits over perioral use. Systematic Medication Administration. The benefits of the above include the potential for bypassing the first pass effect and circumventing some disadvantages. In the gastrointestinal tract, pre-systemic elimination takes place, with the effectiveness of this varying between drugs being metabolized. Drug uptake [1]. There could be the risk of irritation and permanent modification of the nasal delivery system.Besides the considerable variation in mucus secretion from and between individuals, it should be noted what effect this variation has on the general activity of the nasal mucosa. Affect drug absorption from this site. Although the rectal, vaginal, and ocular mucosa each have advantages, they also possess some disadvantages. The inability of these sites to accept patients limits their usefulness to local application alone, as opposed to general use. Systemic delivery of medication. The oral cavity is very acceptable to patients and has smooth, healthy mucosa. Much more porous and generously supplied with nutrition and having an abundant blood supply, it is robust and shows rapid healing properties after stress or trauma [1].The lack of Langerhans cells [2] in the oral mucosa renders it less vulnerable to possible allergens. The oral mucosal drug delivery systems are easily accessible and patient-friendly [1]. The total surface area. The oral cavity is nearly 100 cm long. [3]: The mucosal membranes of the oral cavity can be divided into five different regions. As for the floor of the mouth (sublingual), the cheeks (buccal mucosa), the gums (gingival), the palate (palatal mucosa), and the soft palate. The lips are bordered. While less permeable than the rest of the body's tissues, the buccal mucosa is nonetheless permeable to some substances. The sublingual mucosa Is not as good at delivering the drug fast as the mucosa located under the tongue, hence the drug's slower onset of action. The buccal region contains a vast and smooth area which is not capable of easy movement, thus it is a good site for the insertion of. Retentive System. These characteristics make the buccal mucosa a more appropriate site for prolonged systemic administration and transport of drugs [4] Tetracyclines are a broad group of antibiotics, and they initially came into use in medicine in the late 1940s [5-9]. They are protein synthesis inhibiting antibiotics. Another mechanism has been suggested to be associated with the capacity of Tetracyclines to neutralize reactive oxygen radicals produced by neutrophils and thus prevent further tissue destruction. Thus, Tetracyclines could have broad proteolytic activities. It is well known that Tetracyclines are anticollagenase in nature independent of their antibacterial action [9]. Tetracycline hcl is broad spectrum in activity and inhibits both gram positive and gram negative bacteria, such as beta- lactamase producers, which make penicillin less effective. Tetracycline hcl has been shown to be active against most popular periodontopathic bacteria, with special emphasis on prevotella intermedia and prohormones gingivalis [8].

Dosage forms for mucoadhesive drug delivery must be compact and flexible enough to be tolerable to patients and cannot be irritating. High capacity for carrying drugs, unidirectional release of the drug (if possible), good mucoadhesiveness, smoothness of surface, lack of taste, and ease of application are other characteristics of an ideal mucoadhesive dosage form. Erodible products are useful in the sense that system retrieval at the end of desired dosing interval is not needed. Several mucoadhesive dosage forms pertinent to the current subject have been formulated for various drugs. A number of peptides, such as Thyrotropin-releasing hormone (Trh), insulin, octreotide, leuprolide, and oxytocin, have been administered through the mucosal route, but with comparatively low bioavailability (0.1–5%),[10] due to hydrophobicity and high molecular weight, along with the innate permeation and enzymic barriers of the mucosa.

The formulation of sustained release dosage form Is able to release the drug slowly over a long period of time, but it still requires more in order to achieve a sustained action. They may be flushed away from the absorption site before the drug content is emptied. Alternatively, the mucoadhesive dosage form will serve both the activities of sustained release and the residence of the dosage form on the absorption site. Here, our review is aimed at emphasizing some of the major features of mucoadhesive drug delivery systems.

Advantages of Mucoadhesive drug delivery system

Mucoadhesive delivery systems provide several benefits over other oral controlled release systems due to their ability to prolong the residence time of drugs in the gastrointestinal tract .

- Targeting and localization of the dosage form at a specific site.
- Also, the mucoadhesive systems are known to provide intimate contact between dosage form and the absorptive mucosa, resulting in high drug flux at the absorbing tissue.

Mucus Membrane:

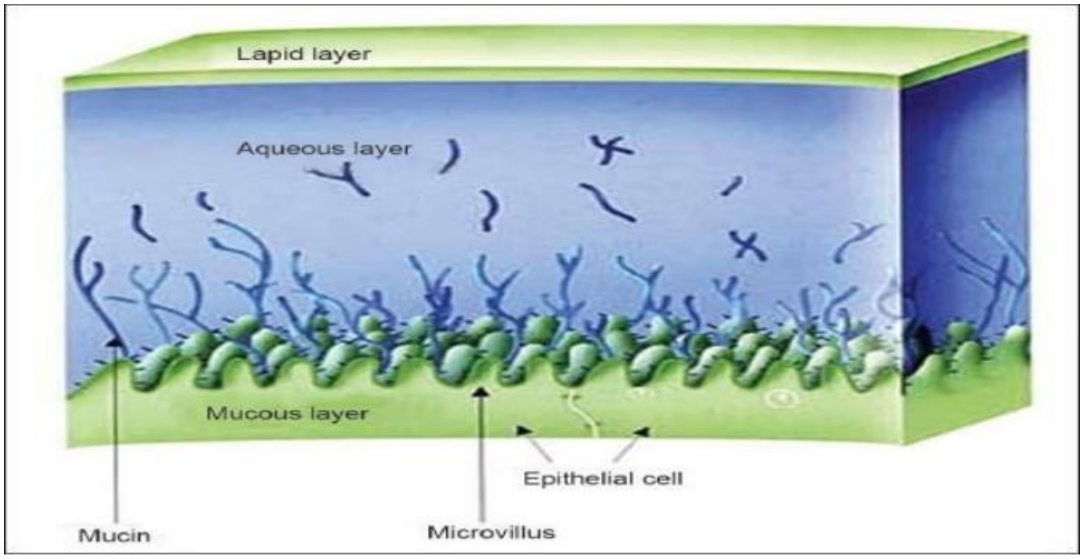


Fig 1 : Structure of Mucus Membrane

Mucus membranes, or mucosae, are the moist surfaces lining the walls of various body cavities, the gastrointestinal and respiratory tracts. Above an epithelial layer, there is a layer of connective tissue called the lamina propria. The surface of the epithelial layer is generally kept moist due to the existence of a layer of mucus. The epithelia are either single layered (e.g. The stomach, small and large intestines and bronchi) or multi-layered/stratified (e.g. In the esophagus, vagina and cornea. Mucus exists either as a gel coat on the mucosal surface or in a soluble or suspended state within the mucus. The chief constituents of all mucus gels are mucin glycoproteins, lipids, inorganic salts and water, the last constituting over 95% of their weight, and thus forming a very hydrated system.[5] the key functions of mucus are protection and lubrication.

Mechanism of Mucoadhesion

The mucoadhesion process is usually classified into two phases: the initial contact phase and the second consolidation phase [figure 2]. In the first phase, there is interaction between the mucoadhesive and the mucus membrane, which results in swelling and expansion of the formulation, creating a strong bonding with the mucus layer. During the consolidation stage [figure 2], the mucoadhesive components are actuated by the availability of moisture. The availability of moisture weakens the system, allowing the mucoadhesive molecules to release and create bonds through weak van der Waals and hydrogen bonds. Fundamentally, there are two theories accounting for the consolidation step: the theory of diffusion and the dehydration theory. This interaction is based on the diffusion theory such that the mucoadhesive molecule and the glycoproteins of the mucus interact via interpenetration of their chains and establishment of secondary bonds. For this interaction to occur, the mucoadhesive device must have properties that enhance chemical and mechanical interactions. For instance, molecules having hydrogen bond building groups (–OH, – COOH an anionic surface charge, high molecular weight, flexible chains and surface-active Behaviour, which aid in spreading across the mucus layer, can exhibit mucoadhesive properties.

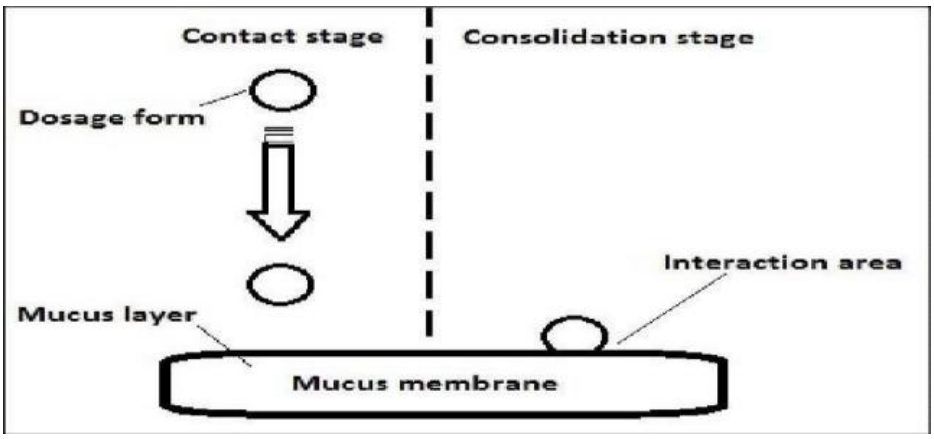


Fig 2 : Mechanism of Mucoadhesion

Mucoadhesion Theory

It is difficult to comprehend the mucoadhesive process, and numerous theories have been proposed to account for the mechanisms involved. Theories put forward include mechanical interlocking, electrostatic, diffusion interpenetration, adsorption, and fracture processes.

Wetting Theory

The wetting theory can be applied to liquid systems which naturally attract the surface and hence spread and wet it. This tendency can be found by using measurement techniques such as the [figure 3]. For good spread ability, the contact angle must be zero or nearly so. The spreadability coefficient, SAB, may be determined from the difference of the surface energies γA and γB the interfacial energy γAB as shown in the equation presented below

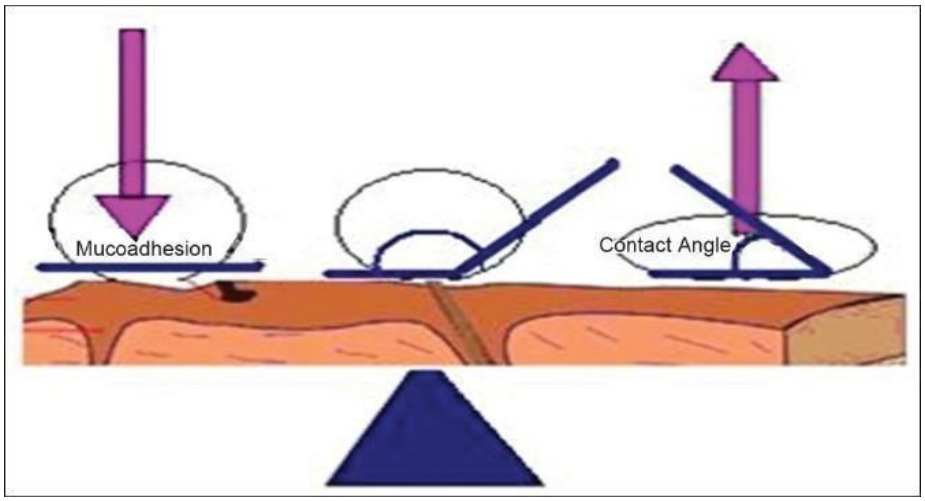


Fig 3 : Wetting theory

PLAN OF WORK

1. Preparation of Mucoadhesive Patch by Chitosan Solution

- Preparation of Chitosan solution

- Addition of plasticizers
- Drug incorporation
- Casting the film

2. Preparation of Standard Curve of Tetracycline Hydrochloride

3. Antimicrobial Studies

- Preparation Of Culture Media
- Staining
- Incubation
- Microbial Studies
- Zone Of Inhibiton

4. In vitro Drug Release

- Preparation of phosphate buffer
- Placing patch in USP apparatus
- Withdrawal sample at specific intervals
- Analyze sample in UV Spectrophotometer

5. Ex-vivo Mucoadhesion Force

- Prepare fresh mucosal tissue
- Attach patch to mucosa
- Apply initial preload for fixed time
- Measurement of force

6. Measurement of Mucoadhesion Time

- Place the mucoadhesive patch in fresh tissue
- Immerse setup in phosphate buffer (pH 6.8) at 37 ± 0.5°C.
- Record the time

Materials requirement: Tetracycline Hydrochloride, Chitosan, Acetic Acid, Glycerine, and the water used throughout all the experiments was HPLC grade. All reagents were of pharmaceutical grade and used as supplied without further treatment. Instruments Digital analytical balance, magnetic stirrer, Hot Air Oven, Water Bath

Methods of preparation:

Preparation of Mucoadhesive patch by Solvent Casting Method

The solvent casting method was used to develop the Mucoadhesive patch. Human and glass trituration was used to accurately measure and combine all ingredients. A magnetic agent was gradually introduced into the solvent system while mixing the prepared mixture. The stirring process continued until the solution became transparent. The solution was then quantitatively transferred to a Petri-dish (glass) with 6 cm diameter. The Petri-dishes were rotated using an inverted core to control the solvent evaporation process. These samples were left undisturbed for a period of 1-2 days at a

temperature range from 20 to 50 degrees Celsius based on the solvent system. A careful drawing process on the Petri-dish produced small spots which measured 15 mm in size with a 20 mm diameter and 0.2-0.3 mm thickness.

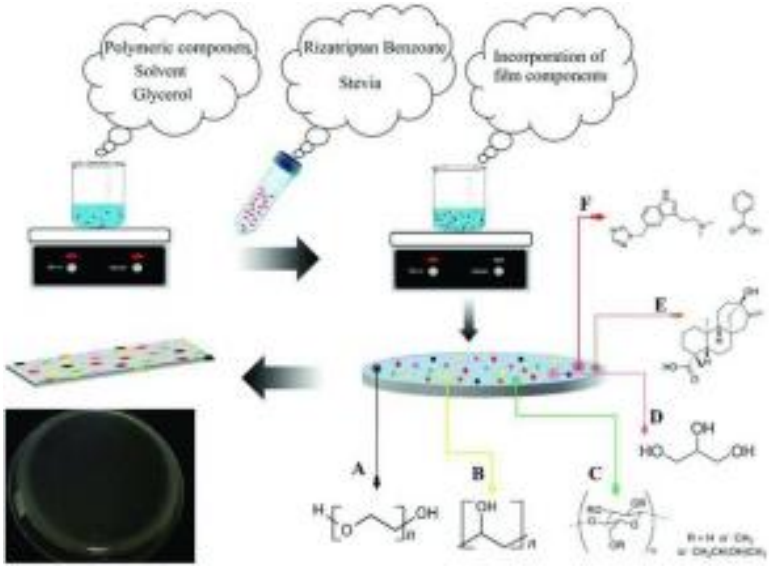


Fig 8: Preparation of Mucoadhesive Patch by Solvent Casting Method

Method for Preparation using Chitosan solution

Preparation of Chitosan Solution: Weigh an appropriate amount of chitosan (usually 1–2% w/v).Dissolve it in 1% acetic acid solution with continuous stirring. Stir for 4–6 hours or until a clear solution is obtained. Allow it to stand overnight to remove air bubbles.

Addition of Plasticizer: Add glycerin or PEG 400 (10–30% w/w of chitosan) to enhance flexibility. Stir until completely mixed.

Drug Incorporation : Tetracycline Hydrochloride was dissolved or dispersed in the chitosan solution. Ensure uniform mixing to avoid dose variation.

Casting the Film: Pour the final solution into a Petri dish or flat mold.Allow it to dry at room temperature or in an oven at 40–45°C for 24–48 hours.

Peeling and Cutting: Carefully peel off the dried film. Cut into desired sizes (e.g., 2 cm × 2 cm) using a sterile blade.

Table 1: Various Formulation of Mucoadhesive Patch

Formulation	Plasticizer Type	Chitosan	Plasticizer Amount	Tetracycline
F1	Glycerin	2g	0.4 g (20% w/w)	100mg
F2	Glycerin	2g	0.6 g (30% w/w)	150mg
F3	PEG 400	2g	0.4 g (20% w/w)	100mg

F4	PEG 400	2g	0.6 g (30% w/w)	200mg
F5	Glycerin + PEG 400	2g	0.2 g + 0.2 g (each 10%)	100mg
F6	None	2g	-	100mg
F7	Glycerin	2g	0.2 g (10% w/w)	50mg
F8	PEG 400	2g	0.3 g (15% w/w)	250mg

Preparation of Standard Curve

- Prepare stock solution of Tetracycline Hydrochloride (e.g., 100 µg/mL).
- Dilute the stock to obtain standard solutions of known concentrations (e.g., 2, 4, 6, 8, 10 µg/mL).
- Measure the absorbance of each solution using a UV-Visible spectrophotometer at the λmax (wavelength of maximum absorption).
- Plot a graph of Concentration (µg/mL) on the X-axis vs. Absorbance on the Y-axis.
- Draw the best-fit line and derive the linear regression equation (e.g., Y = mx + c).
- Use the equation to determine the concentration of unknown samples by their absorbance values.

Antimicrobial activity:

Materials required:

Prepared mucoadhesive patches containing Tetracycline HCl, Nutrient agar (for bacteria),Sabouraud Dextrose Agar (for Candida *albicans*), Standard antibiotic discs (positive control), Sterile Petri dishes, Inoculating loop, Sterile forceps,Incubator (set at 37°C for bacteria, 28–30°C for fungi),Bacterial cultures: E. coli, B. subtilis, S. aureus, Fungal culture: Candida *albicans*

Procedure:

Preparation of Culture Media: Prepare Nutrient Agar for bacterial strains. Prepare Sabouraud Dextrose Agar for Candida albicans.Sterilize the media by autoclaving at 121°C for 15 minutes. Pour the sterilized media into sterile Petri dishes and allow to solidify.

Inoculation of Microorganisms: Prepare standardized microbial suspensions (equivalent to 0.5 McFarland standard).Swab each plate evenly with the respective microbial culture using a sterile cotton swab.

Placement of Patches: Using sterile forceps, place the test mucoadhesive patch samples on the surface of the inoculated agar plates.Place positive control (standard antibiotic disc) and negative control (blank patch without drug) on the same plate for comparison.

Incubation: Incubate bacterial plates at 37°C for 24 hours. Incubate fungal plates at 28–30°C for 48 hours.

Observation and Measurement: After incubation, observe the plates for zones of inhibition (clear area around the patch).Measure the diameter of each zone in millimetres (mm) using a ruler or caliper.

In-vitro Drug Release

In vitro release of tetracycline HCL from the matrices through a dialysis membrane was examined using Franz-type cells with an effective spread area of 2.3 cm². We maintained 15 mL of pH 7 phosphate buffer solution at 37 °C while stirring at 100 rpm; this served as the receptor medium. The matrices, which acted as the donor phase, were kept in contact with the dialysis membrane. The backing layer faced the donor box, and the adhesive film faced the receiver compartment sealed with an O-ring. At set time intervals, we withdrew 3 mL samples from the received phase for analysis and replaced them with an equal amount of fresh buffer to keep the sink condition stable. We measured the amount of tetracycline HCL and cavacrol at 275 nm and 283 nm using a UV spectrophotometer . The analysis method used was the spectra-first derivative method. This method was validated, and each release test was performed at least three times. UV scans of placebo solutions showed no absorption at the analytical wavelength

Ex-Vivo Mucoadhesive Force:

The mucoadhesive strength was determined by measuring the force of adhesion and the ex- vivo adhesion time. These are the most common parameters studied to find adhesive properties. The two- arm-balance method reported by Parodi [26] was used to evaluate the bioidacification of films. A fresh rabbit was fixed at the bottom of a small beaker placed inside a larger beaker [a large beaker, 2 × 2 cm, and 2 mm thick]. The Krebs solution was poured into the large beaker, covering the upper surface of the mucosa. The patch was attached to the upper clamp, and the stage was gradually raised until the patch touched the mucosa. A contact time of two minutes provided the best mucoadhesive strength. Increasing the contact time did not affect the mucoadhesive strength, but decreasing it reduced the mucosa power. This reduction was due to insufficient time for the polymer chains to mix with the mucus. After five minutes of preload time, a weight [g] was added to the other side of the balance until the film separated from the buccal mucosa. The weight [g] needed for separation was recorded. The method was valid, and average values were noted after three experiments.

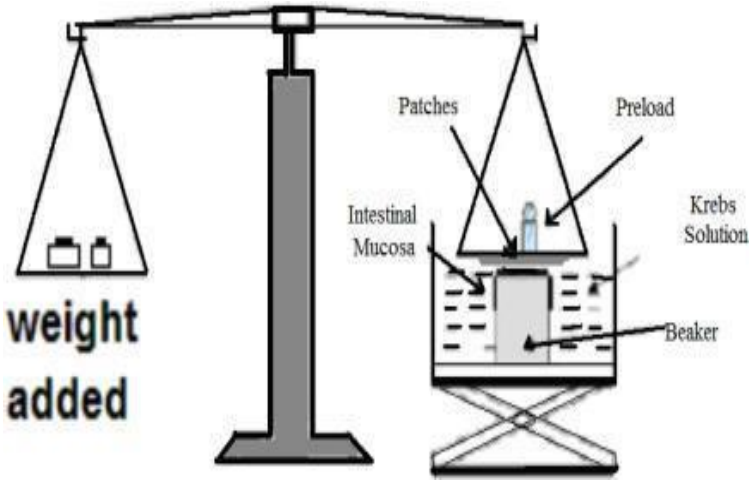


Fig 9: Measurement of Mucoadhesive Force

Measurement of Mucoadhesion Time:

The mucoadhesive performance of the patch was evaluated using rabbit buccal mucosa tissue measuring 2 × 2 cm and 2 mm thick. Researchers recorded the time taken to separate the mucosal section in a well-prepared beaker for the film, which was used to assess the mucous performance. The freshly cut tissue was fixed to the edge of the beaker with glue. Before connecting the buffer, films were attached to the buccal mucosal tissue with light pressure of about 0.5N for 20 seconds. The beaker was then filled with 800 mL of phosphate buffer and placed at a temperature of 37 °C. A stirring

rate of 150 rpm was maintained to monitor the buccal and saliva movement. They recorded the time it took to separate the film from the mucosal tissue over 12 hours. The average values were reported after repeating the experiments three times

Percent Swelling:

The patch, designated as [W1], was weighed and placed in a separate tested tube. This tube was connected to fake saliva, which consisted of 2.38 g Na2HPO4, 0.19 g KH2PO4, and 8 grams per liter of distilled water along with phosphoric acid at 37 °C and 0.5 °C to 0.8 °C. After 2 hours, the patch from the test tube was taken out, and the excess surface water was carefully removed using filter paper. The swollen patch [W2] was then measured using the following equation –The experiments are run in triplicates.

Physical characteristics of the patches

$$\text{Swelling Index} = \frac{\quad}{W1} \times 100$$

Folding endurance :

The folding of the patch was determined by repeatedly turning a patch at one place until it was broken or broken without broken.

Surface pH of the films :

For surface pH determination, three films from each patch were kept at room temperature in contact with 1 mL of distilled water for 2 hours. The pH was measured by placing the electrode on the patch surface and letting it stabilize for 1 minute.

Drug content uniformity :

Select 3–6 patches randomly from a batch. Dissolve each patch in a known volume (e.g., 100 mL) of a suitable solvent under stirring or sonication until complete dissolution. Dilute the filtered solution appropriately to bring the concentration within the detectable range of the spectrophotometer or HPLC.Measure the absorbance using a UV-visible spectrophotometer at the drug's λmax. Alternatively, perform an assay using HPLC if more Precision or multiple drug components are involved. Calculate the drug content per patch or per cm^2.

Thickness, weight uniformity, and stability :

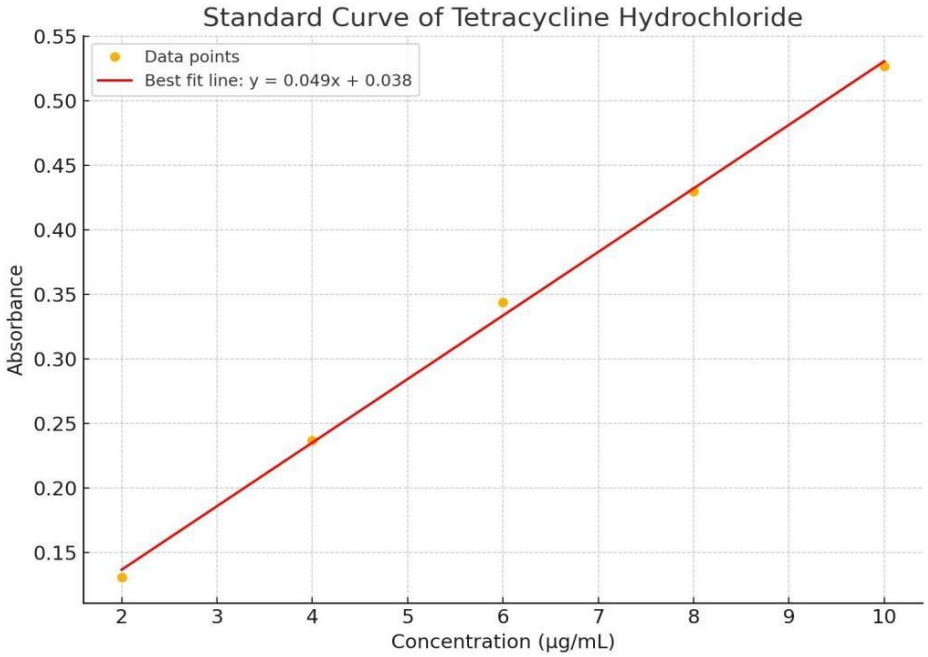
Select at least 3–5 patches randomly from the batch.Measure the thickness at three different points (centre and two edges) on each patch.Calculate the average thickness and standard deviation. Select 10 patches randomly. Individually weigh each patch using the analytical balance. Calculate the mean weight and % deviation from the mean

RESULT AND DISCUSSION

Standard Curve :

Table 2 : Standard curve

Concentration (µg/mL)	Absorbance
2	0.131
4	0.237
6	0.344
8	0.43
10	0.527



Graph 1: Standard Curve

Absorbance (Y) = 0.049x + 0.038

The linearity confirms that Beer-Lambert's law is followed. The equation can be used to calculate the unknown concentration of Tetracycline Hydrochloride in test samples by measuring their absorbance.

Antimicrobial activity:

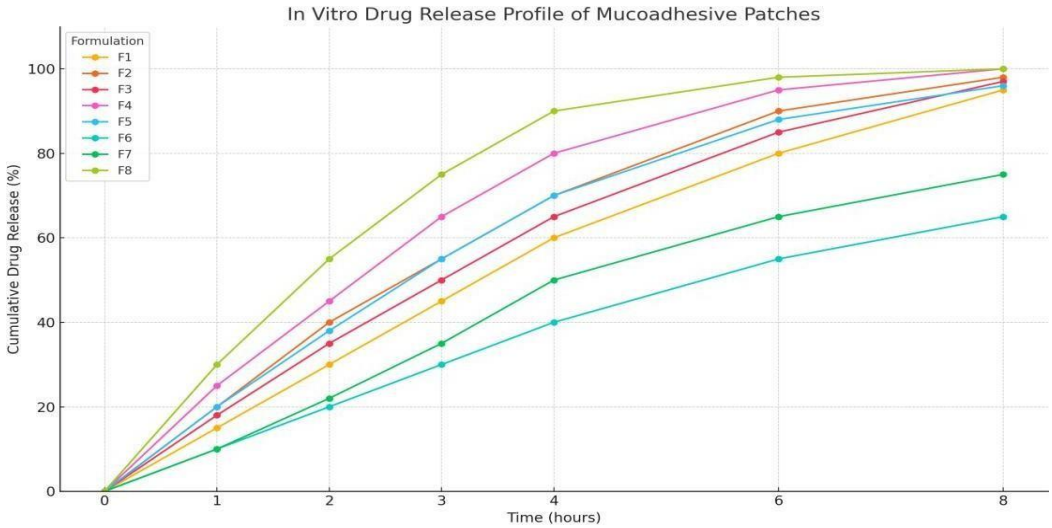
Post-incubation, the diameter of the zone of inhibition surrounding each well was measured in millimetres (mm) using a transparent ruler or Vernier caliper. A tests were performed in triplicate to ensure reproducibility, and the mean values were recorded.

SL NO	Microorganism species	Concentration (mg/mL)	Mucoadhesive patch Tetracycline hydrochloride (mm)	Chloramphenicol (mm)
1	Escherichia coli	5	2.5	3.2
2	Bacillus subtilis	5	2.0	2.3
3	Staphylococcus aureus	5	4.2	2.5
4	Candida albicans	5	3.0	2.2

Table 3 : Antimicrobial activity of mucoadhesive patch containing tetracyclin hydrochloride and Chloramphenicol against Pathogenic microorganism

Fig 10: Antimicrobial activity

In vitro Drug Release:

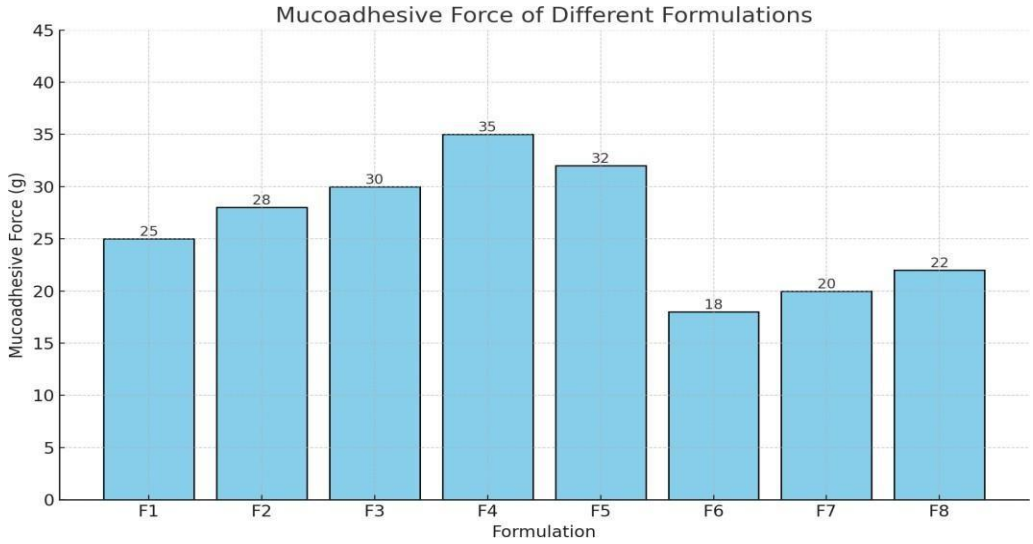


Graph 2 : In vitro Drug release of Mucoadhesive Patches

The graph illustrates the cumulative percentage of drug release over 8 hours for eight different mucoadhesive patch formulations (F1 to F8), each varying in plasticizer type, amount, and drug load.

- **F8** formulation exhibited the fastest and highest drug release (100% by 6– 8 hours).The high drug load and PEG 400 likely facilitated rapid diffusion, resulting in a burst release effect. Ideal for immediate therapeutic action.
- **F4** released 95–100% of the drug within 8 hours. The higher plasticizer content (30% w/w) and PEG 400 improved the patch's permeability and flexibility. Suitable for efficient and sustained delivery.
- **F6** shows the slowest release due to brittleness and lack of plasticizer.

Ex vivo Mucoadhesive force :

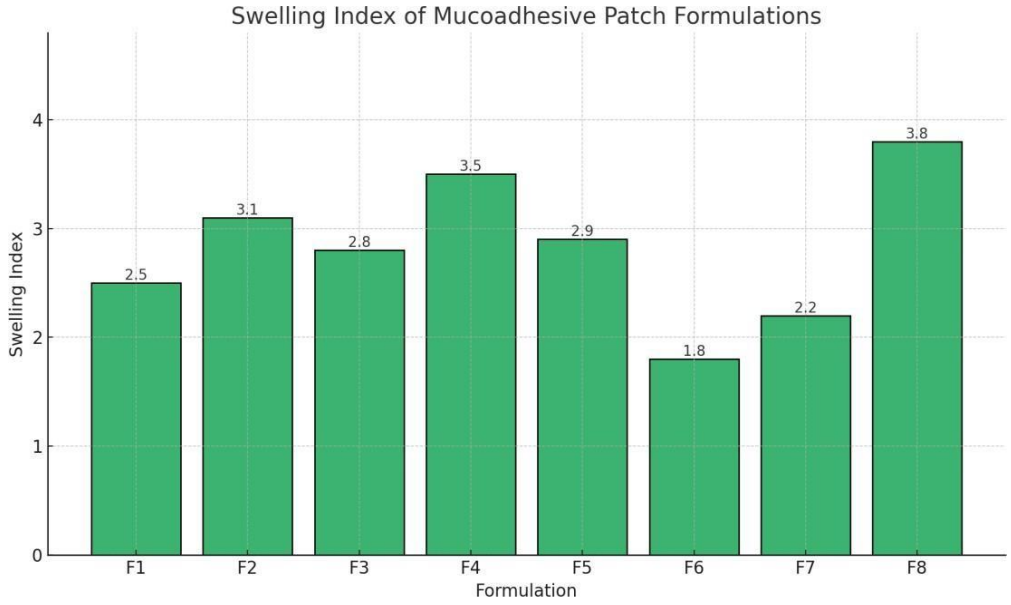


Graph 3 : Mucoadhesive force of different formulations

- F4 (PEG 400, 30%) had the highest mucoadhesive force (35 g), indicating excellent tissue adhesion.

- F5 (Glycerin + PEG 400) and F3 (PEG 400, 20%) also showed strong adhesion (32 g and 30 g respectively).
- F6, which lacks any plasticizer, had the lowest adhesion (18 g), confirming poor mechanical and adhesive properties.
- F1, F2, F7, F8 showed moderate mucoadhesion between 20–28 g.

Swelling index



Graph 4: Swelling index of Mucoadhesive patches

- F8 showed the highest swelling index (3.8), likely due to high PEG 400 content, enhancing water uptake.
- F4 and F2 also exhibited high swelling indices (3.5 and 3.1, respectively), suggesting good hydration capacity.
- F6, with no plasticizer, had the lowest swelling index (1.8), reflecting poor flexibility and low water absorption.
- Formulations with moderate plasticizer levels (F1, F3, F5) showed intermediate swelling behaviour.

CONCLUSION

A mucoadhesive patch made of Tetracycline HCl can deliver drugs in a targeted and regulated way, which is useful for treating oral or skin infections caused by bacteria. A suitable polymer, such as chitosan, and a compatible plasticizer can be used to make a stable and flexible film that can hold drugs well and stick to mucosal surfaces for a long time. The patch sticks well to the skin and keeps the drug there for a long time, which makes it more effective and reduces the harm to other parts of the body. By including Tetracycline HCl in the mucoadhesive patch, the targeted antibacterial action against pathogens such as E. The drug release and mechanical properties of the drug-coated stents were tested in both laboratory and animal experiments. The proposed patch has the potential to be a more effective and convenient way of delivering drugs compared to traditional methods. This research provides a basis for future studies, such as clinical trials, stability improvement, and patient compliance evaluation, to promote the development of mucoadhesive drug delivery systems that utilize antibiotics like Tetracycline HCl.

REFERENCES

1) Rathbone MJ, Hadgraft J. Absorption of drugs from the human oral cavity. Int J Pharm.1991, 74:9-24.
2) Bodde HE Devries, ME Junginger HE. Mucoadhesive polymers for the buccal delivery of peptides structure-adhesiveness relationships. J control Rel.1990, 13: 225-231.
3) Hoogstraate AJ, Verhoef JC, Tuk B, Pijpers A, et al. Buccal delivery of fluorescein isotjiocyanate-dextran 4400 and the peptide drug buserelin with glycodeoxycholate as an absorption enhancer in pigs. J. Control Rel.1996, 41: 77-84.
4) Shojae AH et al., 1998. Buccal mucosa as a route for systemic drug delivery. A Review, J Pharm Pharmaceut Sci.1998, 1(2): 66-73.
5) Goodson JM, Holborow D, Dunn RL, Hogen P, Dunham S. Monolithic tetracycline- containing fibers for controlled delivery to periodontal pockets. J Periodontol. 1983;54:575–579.
6) Esposito E, Ortesi R, Cervellati F, Menegatti E, Nastruzzi C. Biodegradable microparticles for sustained delivery of tetracycline to the periodontal pocket: formulatory and drug release studies. J Microencapsul. 1997;14:175–187.
7) Seymour RA, Heasman PA. Biodegradable microparticles for sustained delivery of tetracycline to the periodontal pocket: formulatory and drug release studies. J Clin Periodontol. 1995;22:22–35.
8) Chambers HF. General principles of antimicrobial therapy. In: Bruton LL, editor. In Goodman and Gilman's The Pharmacological Basis of Therapeutics. 11th Ed. McGraw Hill; USA: 2006. Pp. 1102–1104.
9) Goodson JM, Tanner A. Antibiotic resistance of the subgingival microbiota following local tetracycline therapy. Oral Microbiol Immunol. 1992;7:113–117. Veuillez F, Kalia YN, Jacques Y, Deshusses J, Buri P. Factors and strategies for improving buccal absorption of peptides. Eur J Pharm Biopharm. 2001;51:93–109.
10) Punitha S, Girish Y. Polymers in mucoadhesive buccal drug delivery system: A review. Int J Res Pharm Sci. 2010;1:170–86