International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.4, No.1, pp 422-426, Jan-Mar 2012

A Novel, Potent, Bio-Film Former from the Seeds of *Buchanania lanzan* for formulating Tobramycin Occuserts.

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Abstract : The aim of the research work was to isolate a novel bio material from the seeds of Buchanania Lanzan and to evaluate its bio film forming ability by formulating various ophthalmic films using PEG 400 as plasticizer and biomaterial as bio film former. The bio polymer was isolated from the seeds of Buchanania Lanzan by simplified economical method. Four formulations were prepared using bio film former in different ratios by film casting technique. Acute toxicity studies were done in rats according to OECD guidelines .the formulated ophthalmic films were subjected to various evaluation parameters like weight variation , uniformity thickness , folding endurance, hardness, surface ph, swelling index and invitro release studies. The drug release studies from the formulated ophthalmic films exhibited a promising stability, swelling index, folding endurance and sustainability for a period of 8 hrs. The conclusion was drawn that the isolated bio film former act as a novel film former for formulating various ophthalmic films.
Key words: ophthalmic films, tobramycin, *Buchanania Lanzan*.

INTRODUCTION:

The current aim of the research work is to isolate a novel bio material from the seeds of Buchanania Lanzan and to evaluate its bio- film forming ability by forming various tobramycin ophthalmic films using PEG 400 as plasticizer and bio- material as bio film former. The bio- material was isolated from the seeds of Buchanania Lanzan by simplified economical method.

Buchanania Lanzan consists of magnesium, iron, calcium, phosphorous and potassium. It is used in the treatment of glandular swelling of neck and act as a brain tonic and also used in itching and blemishes on face. Tobramycin is an amino glycoside antibiotic used in the treatment of various bacterial infections especially gram negative bacteria.

The ocular route of drug delivery has become popular recently and its importance has been extensively pointed out. To achieve controlled and constant release of drug, ocular systems require suitable rate controlling membranes and drug reservoirs. The permeability of drugs through the polymeric free films is dependent on the characteristics of the polymer, the casting solvent, and the plasticizers used. Preparation of polymeric ocular films for ocular requires plasticizer for various reasons: to reduce the brittleness, to impart flexibility, to increase strength, and also to improve adhesiveness of the films with surfaces or membranes. Plasticizers interpose themselves between the polymer chains and interact with the chains to extend and soften the polymer matrix.

Local therapy is preferred over systemic therapy for the eye to avoid risk of eye damage from high bold concentrations of the drug. Most ocular treatments,

like eye drops and suspensions, call for topical administration of ophthalmically active drugs to the tissues around the ocular cavity. These dosage forms are easy to instill but suffer from inherent drawback that the majority of the medication they contain is immediately diluted in the tear film as soon as the eye drop solution is instilled into the cul de sac. It is then rapidly drained away from the precorneal cavity by constant tear flow and lacrimo-nasal drainage. Therefore, because only a small fraction of the instilled dose is absorbed by the target tissue, concentrated solutions and frequent dosing are required for the instillation of the drug to achieve an adequate level of therapeutic effect[1]. One of the new classes of drug delivery systems, polymeric film ophthalmic drug delivery systems, which are becoming more popular worldwide , release drugs at a pre programmed rate for a longer period by increasing precorneal residence time[2].

MATERIALS

The model drug tobramycin was obtained from Axa laboratories ltd., Roorkee as a gift sample. All the reagents were of analytical grade. Double distilled water was used throughout the study.

ISOLATION OF BIOPOLYMER FROM BUCHANANIA LANZAN SEEDS

Seeds of *Buchanania Lanzan* were soaked in water for 2-3 hrs and the outer cover was removed. The white portion was grounded into a paste and then distilled water was added and filtered through muslin cloth. The milk was centrifuged and the supernatant liquid was separated and acetone was added in equal quantity and kept for 24 hrs. The settled biomaterial was separated by centrifugation for 5 -10 min and the isolated biomaterial was naturally dried and sieved through mesh size 120. The polymer obtained yields about 500 mg.

FORMULATION OF TOBRAMYCIN OPHTHALMIC FILMS USING BIO POLYMER-

Four different formulations were prepared by film casting technique. The films were prepared by making drug polymeric solution in water and then filtered through the muslin cloth to remove the debris. Acetic acid and n-propanol were added as solvents and PEG 400 as plasticizer. The solution was poured over the glass petri dish kept over a uniform surface and allowed to dry at room temperature until a flexible film was obtained[3][4][5].

EVALUATION PARAMETERS[7]:

The ophthalmic films were evaluated for various evaluation parameters :-

- **Physical appearance**
  All the formulated ocular inserts were visually inspected for color and smoothness.
- **Uniformity of thickness**
  The thickness of ophthalmic inserts was determined by using micrometer screw guage. The thickness of each film at different places was determined and the standard deviation was calculated.
- **Weight variation**
  Six inserts of same size from each formulation were weighed individually on electronic weighing balance and the average weights as well as standard deviation were calculated.
  All measurements (thickness and weight) were determined after residual solvent has been removed from samples by storing the films in dessicator with anhydrous calcium chloride at an appropriate 0% RH and 27 ±2 ^{0}c for a week prior to evaluation and testing.

- **Folding endurance**
  The folding endurance is expressed as the number of folds (number of times the insert is folded at the same place) either to break the specimen or to develop visible cracks. This test is important to check the ability of sample to withstand folding. This also gives an indication of brittleness. This specimen was folded in center, between fingers and the thumb and then opened. This was termed as one folding. The process was repeated till the insert showed breakage or cracks in center of insert. The total folding operations were named as folding endurance value

Table no.1 Formulations prepared

Formulation	OF1	OF2	OF3	OF4
Tobramycin(mg)	100	100	100	100
Biomaterial (mg)	100	200	400	600
Acetic acid (mg)	3	3	3	3
n- propanol(mg)	4	4	4	4
PEG 400(ml)	2	2	2	2
Distilled water(ml)	3	3	3	3

- **Surface pH: -**
  Inserts were left to swell in a closed petri dish at room temperature for 30 min. in 0.1 ml of distilled water ph paper was kept on surface and after one min. the color developed was compared with the standard color.
- ***In Vitro* release studies :-**
  The *in vitro* release studies in case of ophthalmic films were performed using dissolution apparatus for 24 hrs in simulated tear fluid (STF) ph 7.4.

RESULTS AND DISCUSSIONS:

PHYSICO CHEMICAL PROPERTIES OF THE BIO MATERIAL:

A novel bio polymer from Buchanania Lanzan was isolated by simplified economical process the yield was 500 mg . the bio polymer obtained was brownish to light brown color with a color changing point of 190-210 ^{0}C. the bio polymer showed positive tests for the carbohydrates and proteins.

EVALUATION PARAMETERS:-

- **Weight variation[8][9]**:- the weights of all the films were found to be in range of 0.003(±0.0074) to0.005(±0.00015) g. the uniformity of weights of the films indicates good distribution of drug polymer and plasticizer.
- **Folding endurance[10]**: - Folding endurance measures the ability of a film to withstand rupture. The folding endurance was measured manually by folding the film repeatedly at appoint until it broke; the breaking time was considered as the end point. Folding endurance was found to be highest for OF4 (202.33±6.6) and lowest for OF1 (103.66±6.0). it was found that folding endurance of the films was increased by increasing the polymer ratio. The folding endurance values of the films were found to be optimal and therefore, the films exhibit good physical and mechanical properties.
- **Surface pH[12]:-** the surface ph of the prepared films was found to be in the range of 6.80 to 7.40. This indicates that the prepared films would not alter the ph of the tear fluid in the eyes and no irritation would occur in the eye after application of the films.
- ***In Vitro* release studies:-** the invitro release data in all the formulation was performed in zero order, zero-first order, higuchi equation in order to evaluate its release mechanism. The result showed the zero first order release pattern. Among the formulations, OF4 had a t50% and t80% of 140 and 170 mins. respectively.

Table 2: Physical properties of the bio material:-

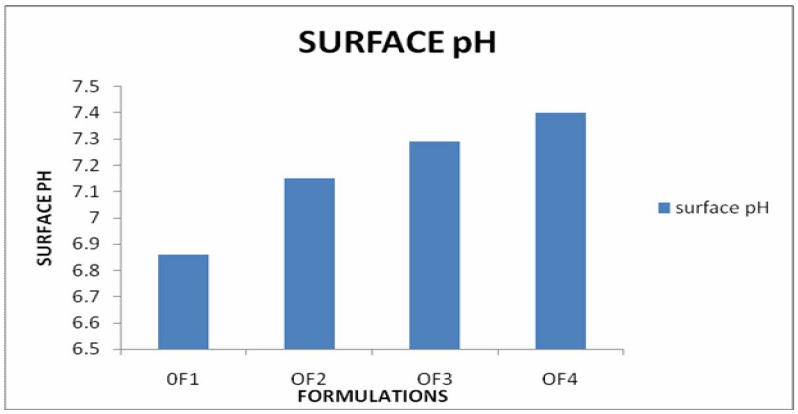
S.No.	Parameters	Observations
1	Color	light brown
2	Odor	Characteristic
3	Taste	Tasteless
4	Solubility	Water
5	Color changing point	190-210 ^{0}c ±10

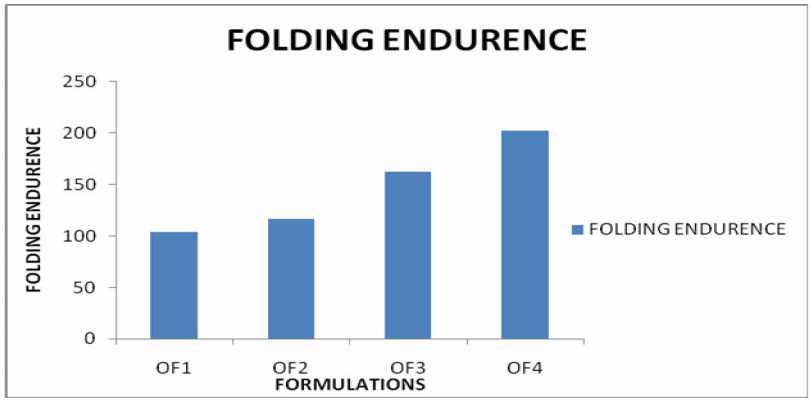
Table 3: Chemical properties of the bio material :

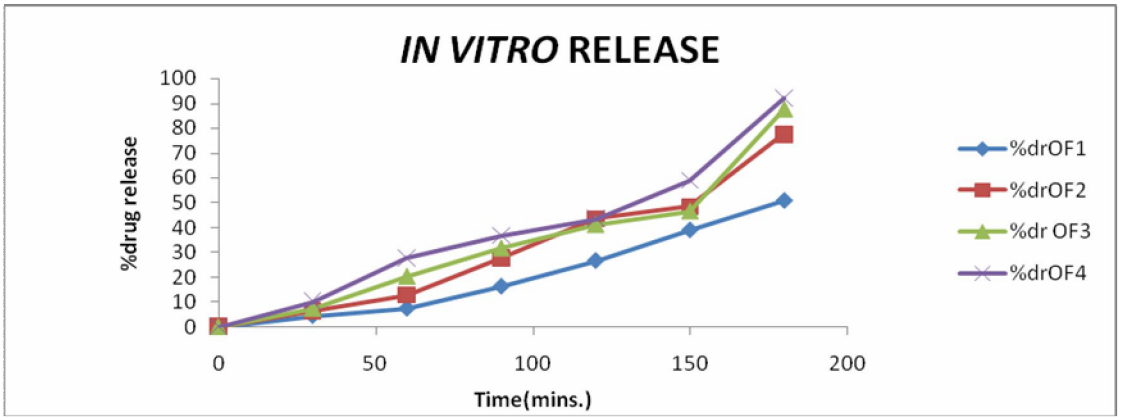
S.No.	Chemical constituents	Observations
1.	Carbohydrate	Present
2.	Protein	Present

Table 4:

S.No.	Parameters	OF1	OF2	OF3	OF4
1.	Weight variation(g)	0.003±0.00074	0.003±0.00074	0.004±0.00083	0.005±0.00459
2.	Thickness (mm)	0.073±0.0017	0.093±0.0015	0.075±0.016	0.129±0.0029
3.	Folding endurance	103.66±6.02	116.66±3.21	162±7	202.33±6.65
4.	Surface ph	6.86	7.15	7.29	7.4







Invitro release study of the ophthalmic films of tobramycin.

DISCUSSIONS:

A novel bio polymer from Buchanania Lanzan was isolated by simplified economical process the yield was 500 mg. the bio polymer obtained was of brownish to light brown colour with a color changing point of 190-210 ^{0}C. The bio polymer showed positive tests for the presence of proteins and carbohydrates. Four different formulations were formulated using different ratios of bio material for the preparation of ophthalmic films of tobramycin. The invitro release data in all the formulations was performed in zero order, first order, higuchi equation in order to evaluate its release mechanism.

CONCLUSION:

Finally the experimental results had shown promising observations in terms of surface pH, folding endurance, weight variation and uniformity in thickness. Here the conclusion was drawn that the isolated bio polymer has shown its potentiality as bio film former for formulating ophthalmic films. The polymer can serve as potential polymer for formulating various drug loaded films.

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