

Netraliner: A novel approach for eye infection

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ABSTRACT: Conjunctivitis is the most common eye infection, which happens in the Conjunctiva part of eye, ciprofloxacin and chloramphenicol are the most widely used and they are the proven drug for the treatment of conjunctivitis. We prepared the sustained release combination of ciprofloxacin and chloramphenicol named as "NETRALINER", it provides the sustained release of the drugs as we used the sustained release polymer HPMC. The combination of ciprofloxacin and chloramphenicol is unique and it's not available in the market and this combination give synergistic effect to kill bacteria and we used the herbal excipients (such as triphala, licorice, Indian berberis) to enhance its action and to provide a pleasant effect to eyes. NETRALINER is not just unique but it give patient compliance as it required less frequency of dose so it cause very less side effect as compared to other formulation. NETRALINER is easy to use as it is having a soft applicator to apply the medicament in the eye easily, the combo of the ciprofloxacin and chloramphenicol is more effective than the single drug. The biggest disadvantage of eye drops is more frequency of dose i.e. (3 to 4 times a day) and the waste of drug due to expulsion of the drops from the eye, the NETRALINER solved these problems as it is having less frequency of dose and no wastage of drugs as there is negligible expulsion from eyes.

Keywords: Netraliner; Ciprofloxacin; Chloramphenicol; Conjunctivitis

I. INTRODUCTION:

If you've used eye drops or eye ointments, you may have experienced the problem of blurry vision and being unable to continue your work due to these conventional dosage forms [1,2,3]. However, these problems are solved by our formulated product "Netraliner" which uses the "NDDS" technique of drug delivery [4]. Our product is essentially a transparent eyeliner (unisex) that delivers drugs from lower eyelid,

where it forms a layer and slowly releases the drug (sustained release) [5,6]. Netraliner is formulated using the latest drug delivery techniques and is an effective solution for these common problems such as conjunctivitis and corneal ulcer [7,8]

Conjunctivitis, also referred to as "pink eye," is an infection or swelling of your conjunctiva, a thin, transparent membrane that covers the white area of your eye and lies over the inner surface of your eyelid. The blood vessels in your conjunctiva become inflamed when you have pink eye. This causes the red or pink coloration of your eyes that is commonly associated with conjunctivitis [9].

Inflammation and swelling of the conjunctival tissue, engorgement of the blood vessels, ocular discharge, and pain are all symptoms of conjunctivitis. Conjunctivitis affects a large number of people globally and is one of the most common causes of office visits to general medical and ophthalmology clinics. It has been reported that non-ophthalmologists such as internists, family medicine doctors, paediatricians, and nurse practitioners diagnose more than 80% of all acute cases of conjunctivitis [10].

A corneal ulcer is a serious and potentially vision-threatening condition that requires prompt diagnosis and treatment. According to a study published in the journal Eye, corneal ulcers affect approximately 30,000 people in the United States each year and can result in significant morbidity and healthcare costs (Gopinathan et al., 2009). Corneal ulcers are often caused by bacterial, viral, or fungal infections, which can occur as a result of injury or trauma to the eye, contact lens use, or underlying conditions such as dry eye or autoimmune diseases. Other risk factors for corneal ulcers include advanced age, diabetes, and a compromised immune system. Symptoms of a corneal ulcer may include eye pain, redness, blurred vision, sensitivity to light, discharge or

tearing, and a feeling of a foreign object in the eye. Diagnosis of a corneal ulcer typically involves a comprehensive eye examination, including an evaluation of the patient's medical history, symptoms, and any contributing factors [11,12].

Ciprofloxacin is an antibiotic medication that is widely used to treat a variety of bacterial infections. It is a member of the fluoroquinolone class of antibiotics, which work by inhibiting the DNA replication process in bacteria, thereby preventing their growth and spread[13]Conjunctivitis (pink eye) and corneal ulcers are among the infections of the eyes that are treated with ciprofloxacin. Ciprofloxacin was discovered to be extremely effective in treating bacterial corneal scarring (corneal ulcers) and was linked to a high rate of clinical cure, according to a study printed in the journal Ophthalmology (Wilhelmus et al., 1996).Eye infections are typically treated with ciprofloxacin eye drops or ointment. The drug reduces inflammation while also eliminating the infection-causing bacteria.[14]

The combination of ciprofloxacin and chloramphenicol is sometimes used in the treatment of bacterial infections, particularly in regions where antibiotic resistance is common. Ciprofloxacin is a fluoroquinolone antibiotic that works by inhibiting bacterial DNA synthesis, while chloramphenicol is a broad-spectrum antibiotic that inhibits bacterial protein synthesis[15].Netraliner, a sustained release combination of ciprofloxacin and chloramphenicol that has a synergistic effect against eye infections like conjunctivitis and corneal ulcers.Netraliner is a semi-solid dosage form with an ideal combination that is applied with an applicator to the lower eyelid and it has synergistic action against a variety of eye infections.This dosage form must be applied to the lower eyelid, where it forms a layer and slowly releases the drug.Netraliner is aiming to achieve a number of goals, including effective

combination, high patient compliance, lower dose frequency, and novel formulation.

Material:1) Ciprofloxacin

2) Chloramphenicol

3) HPMC

4) Extract:

- i. Triphala,
 - ii. Licorice,
 - iii. Indian berberis
- 5) Glycerin

Method of preparation:

Part one:Extraction

• Using 1000 ml of sterile water, we prepared the extraction of Indian berberis, licorice, and triphala from their powder form. The steps we took are listed below.

• Process:

- 1) Weigh and mix the triphala, licorice, and Indian berberis powders into a 1000 ml beaker of sterile water.
- 2) Boil it and maintain the flame for 4 hours and keep stirring occasionally.
- 3) Use muslin cloth to filter the mixture.
- 4) Use this filtrate for formulation in the following step.

Part two: Formulation

1. Pour the extract (Triphala, Licorice, and Berberis) into the beaker.
2. Stir it, then add the first API Ciprofloxacin then add the second API Chloramphenicol.
3. The polymer HPMC is next added gradually, and the mixture is continuously stirred to achieve the desired viscosity
4. Add a small amount of glycerine now, and thoroughly mix.
5. Add glycerine to the volume to bring it up to 10ml.

INGREDIENTS	F1	F2	F3	F4	ROLE
Ciprofloxacin	0.3g	0.3g	0.3g	0.3g	ANTIBIOTIC
Chloramphenicol	0.25	0.45g	0.5g	0.5g	ANTIBIOTIC
HPMC	0.30g	0.22g	0.21g	0.18g	POLYMER
Extract	5ml	5ml	3.5ml	2.5ml	EXCIPIENTS
Glycerin	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml	VISCOSITY ENHANCER



Evaluation Test for Netraliner


Physical parameters:-

- The formulated Netraliner was tested for clarity.

The results are as shown in Table below:

Formulation	F1	F2	F3	F4
Visual Appearance	Light brown colour	Light brown colour	Cream colour	White colour
Clarity	Unclear	Unclear	Clear	Clear

pH Test [16,17]

Formulation	F1	F2	F3	F4
pH	8.5	8	7.5	7
				

Rheological studies:-

The viscosity measurements were carried out using Brookfield viscometer RVDVE model. The spindle of size 07 was attached to the viscometer. The speed of viscometer was kept at 100 RPM. The Netraliner formulation was taken in

4 different beakers. The spindle was submerged in the beaker containing samples and motor was turned on. After waiting for few seconds, the most frequently displayed reading was recorded in cP [18,19]

The final recorded readings are shown in the table below:

Formulations	F1	F2	F3	F4
Readings (incP)	4000cP	4200Cp	4280cP	4680cP
Percentage value	10.0%	10.5%	10.7%	11.7%


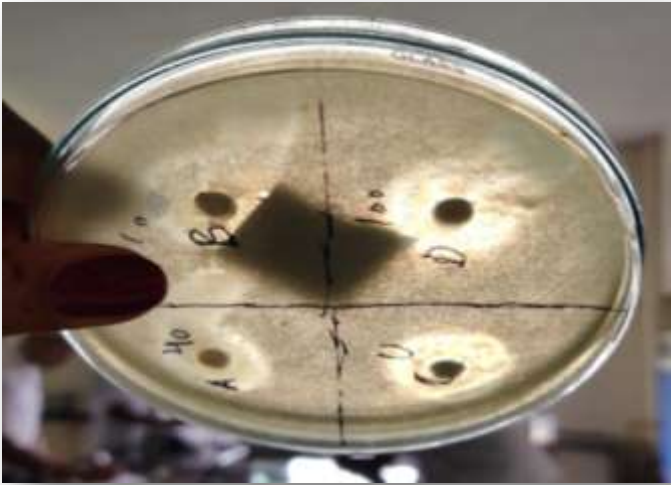


Antimicrobial Activity:-

Cup Plate Method:

Prepare nutrient agar plate inoculated using E.coli organism, with a depth of 4-5mm and then allow it to solidify. Divide the NA plate into four equal portions. Then with the help of a sterile

borer make four cavities one in each portion. Then fill all four cavities with different formulations i.e. F1, F2, F3 & F4 respectively. Then slowly incubate the plates at 37⁰C for 24 hours. After incubation measure the zone of inhibition [20,21]

Before Incubation	After Incubation
	

Irritability test:-

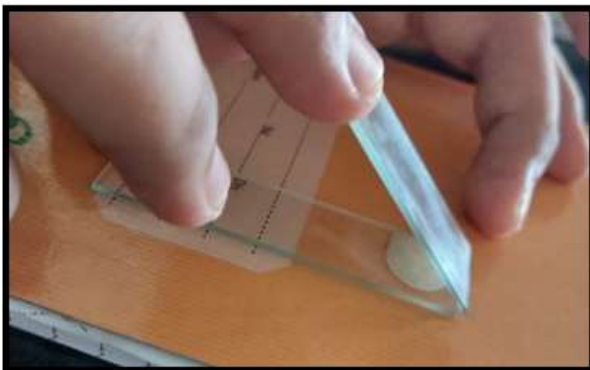
The formulated samples are directly applied topically on the hand for 45mins to determine

whether the Netraliner will cause any local irritation in the skin.



Spreadability Test:- During the experiment, a test sample of a certain mass is placed on a glass plate, and then the other glass plate was tilted (on the glass with sample) forming an angle of 40° and

then tilted glass plate was allowed to spread the sample on the glass plate. Then the distance covered by the sample on plate was measured in cm.



FTIR

1) Chloramphenicol

Peak Position	Group	Class	Peak Details
3567.41	O-H stretching	Hydroxyl group	strong, broad
1569.05	C=C stretching	Aromatic ring	medium
1747.54	-C=O stretching	Ketone group	strong
3567.41	-N-H ₂ stretching	Amine group	medium
1206.00	-O- stretching	Ether group	strong
1569.05	-NO ₂ stretching	Nitro group	strong
753.17	-Cl stretching	Chlorine atom	strong

2) Ciprofloxacin

Peak Position	Group	Class	Peak Details
1700.16	COOH stretching	Carboxylic acid group	strong
1550.16	C=C stretching	Aromatic ring	medium
1700.16	-C=O stretching	Ketone group	strong
3651.49	-N-H ₂ stretching	Amine group	medium
1338.89	-F stretching	Fluorine atom	strong

3)Netraliner

Peak Position	Group	Class	Peak Details
3575.25	O-H stretching	Hydroxyl group	strong, broad
1558.72	C=C stretching	Aromatic ring	medium
1734.00	-C=O stretching	Ketone group	strong
3447.70	-N-H ₂ stretching	Amine group	medium
1266.57	-O- stretching	Ether group	strong
1558.72	-NO ₂ stretching	Nitro group	strong
804.83	-Cl stretching	Chlorine atom	strong
1734.00	COOH stretching	Carboxylic acid group	strong
1623.56	C=C stretching	Aromatic ring	medium
1700.16	-C=O stretching	Ketone group	strong
3447.70	-N-H ₂ stretching	Amine group	medium
1338.89	-F stretching	Fluorine atom	strong
3575.25	-OH stretching	Hydroxyl group	strong, broad
1266.57	-O- stretching	Ether group	strong
3447.70	-CH ₃ stretching	Methyl groups	
2708.42	C-H stretching	Cellulosic backbone	medium
1104.10	C-O-C stretching	Cellulosic backbone	strong
947.70	C-C stretching	Cellulosic backbone	

Drug release

Time (min)	Absorbance of Ciprofloxacin (wl 275.0)	Concentration of Ciprofloxacin (mg/mL)	% Release	Absorbance of Chloramphenicol (wl 278.0)	Concentration of Chloramphenicol (mg/mL)	% Release
0	0	0	0.00%	0	0	0.00%
15	0.112	0.92	20.82%	0.124	0.105	22.82%
30	0.139	0.104	27.14%	0.148	0.113	26.04%
45	0.145	0.109	29.43%	0.165	0.122	28.76%
60	0.174	0.111	30.63%	0.182	0.139	31.36%
75	0.189	0.119	32.31%	0.198	0.154	35.87%
90	0.208	0.125	33.99%	0.217	0.163	37.49%
105	0.217	0.134	36.08%	0.231	0.176	40.21%
120	0.226	0.145	39.02%	0.248	0.185	46.43%
135	0.248	0.157	43.70%	0.263	0.191	48.70%
150	0.256	0.168	48.67%	0.277	0.201	52.67%
165	0.261	0.173	53.00%	0.285	0.207	54.76%
180	0.285	0.182	55.68%	0.301	0.211	56.68%
195	0.296	0.193	56.94%	0.316	0.217	58.44%
210	0.312	0.199	58.00%	0.321	0.219	59.98%
225	0.328	0.206	60.20%	0.334	0.223	61.90%
240	0.339	0.213	62.88%	0.345	0.228	63.54%
255	0.345	0.219	64.27%	0.349	0.233	65.27%
270	0.353	0.225	65.65%	0.354	0.236	66.56%
285	0.358	0.234	69.33%	0.359	0.239	68.33%
300	0.361	0.239	71.72%	0.367	0.242	69.92%
315	0.369	0.244	74.10%	0.372	0.249	71.65%
330	0.372	0.247	76.97%	0.379	0.25	72.06%
345	0.378	0.251	78.06%	0.384	0.257	73.76%
360	0.385	0.256	80.14%	0.388	0.259	74.94%
375	0.389	0.259	82.23%	0.393	0.268	77.23%
390	0.393	0.264	85.58%	0.399	0.276	79.85%
405	0.402	0.269	88.30%	0.405	0.285	80.53%
420	0.406	0.273	90.77%	0.413	0.292	83.67%
435	0.409	0.277	93.05%	0.421	0.298	85.95%
450	0.419	0.279	95.60%	0.434	0.319	89.96%
465	0.422	0.282	97.14%	0.445	0.327	93.74%
480	0.436	0.285	98.42%	0.456	0.345	96.32%

Comparative Study of Netraliner

pH Test :

We evaluated the pH of two marketed Ophthalmic Ointments versus Netraliner.



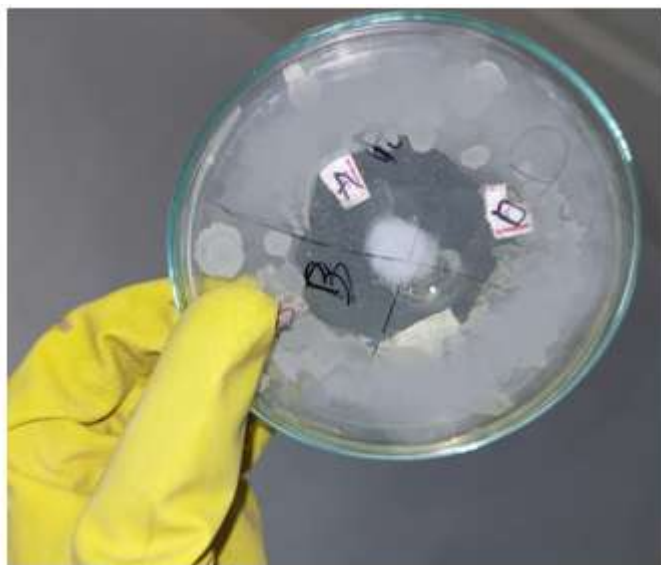
Both the Ointments were neutral in nature [17].

Antimicrobial Test :

We aimed to evaluate the efficacy of two marketed Ophthalmic Ointments versus Netraliner against the

E.coli using the Cup Plate Method of antimicrobial testing .

Antimicrobial Activity of Netraliner



Antimicrobial Activity of Ciprofloxacin and Chloramphenicol Ophthalmic Ointment

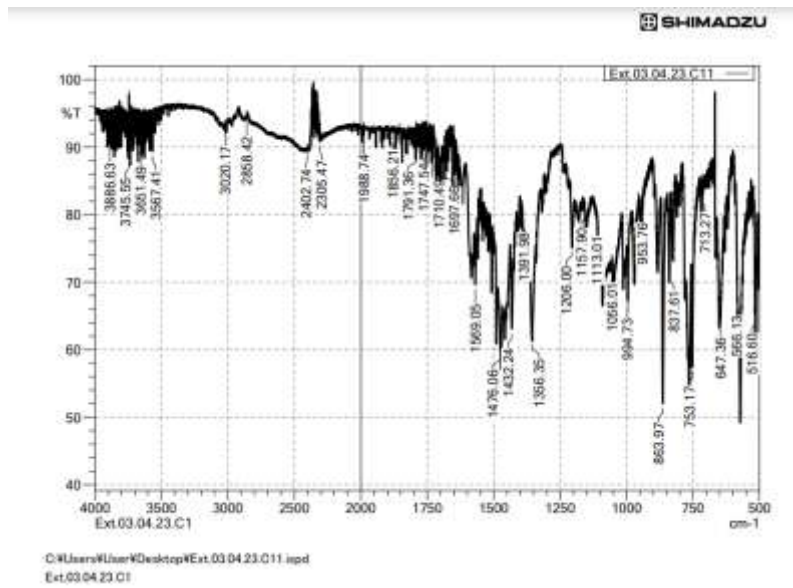
Result:



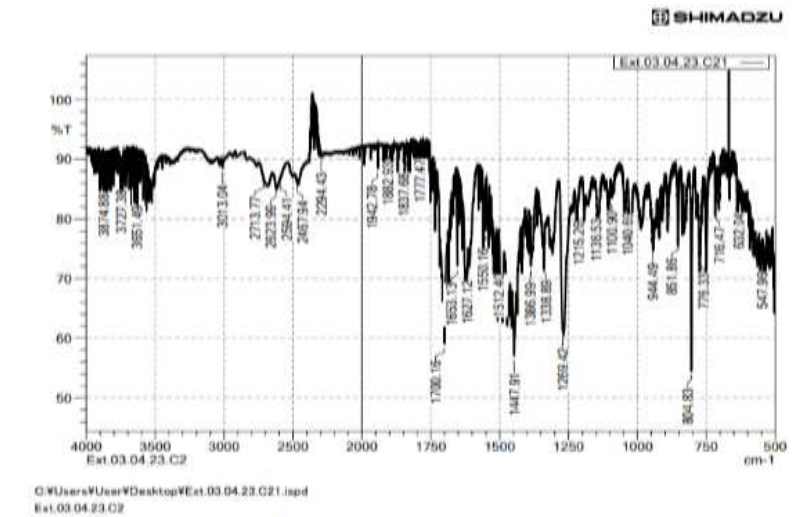
By comparing the two marketed ointment and Netraliner, we noticed that Netraliner had higher efficacy against micro organisms than the marketed ointments [21].

FTIR Graph

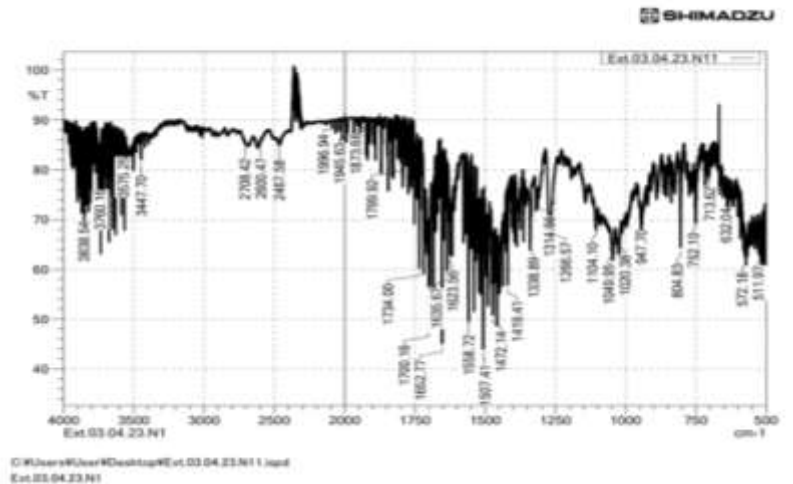
- 1) Chloramphenicol



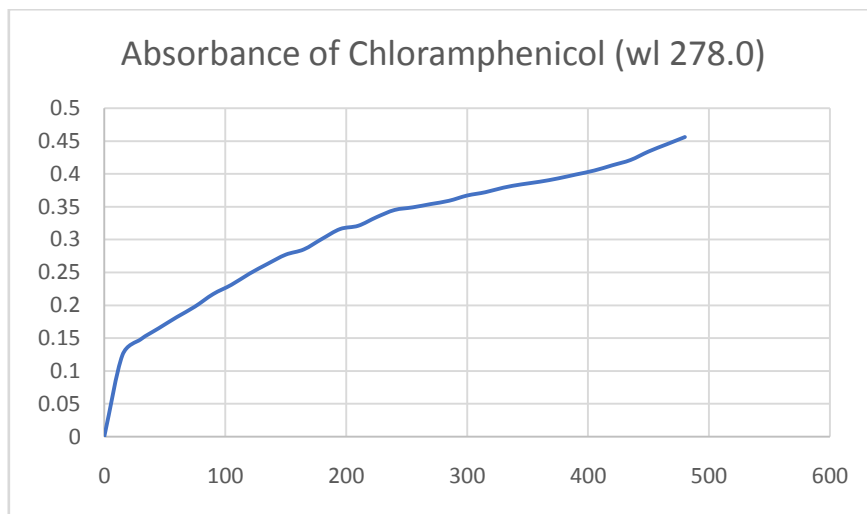
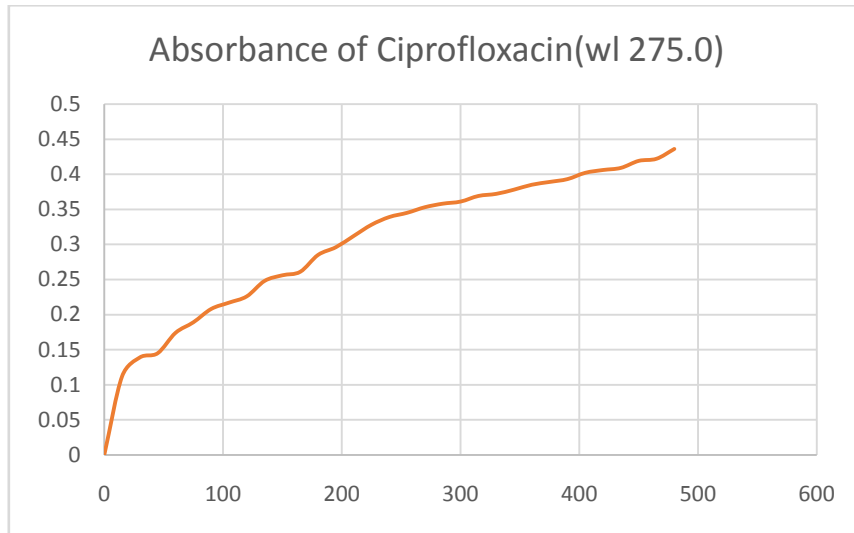
2) Ciprofloxacin



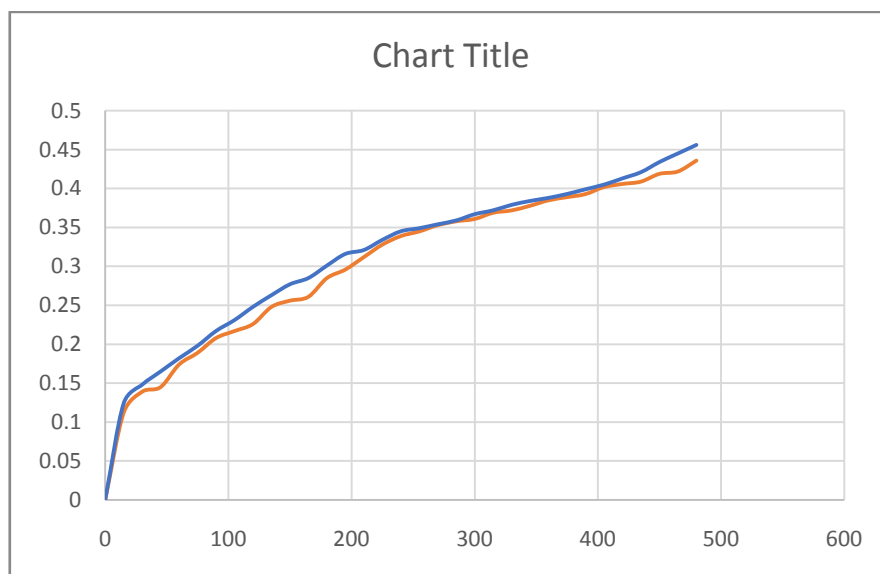
3) NETRALINER



Drug Release Graph (time vs absorbance)



Both drug (API)



II. CONCLUSION:

In summary, a topical application of Netraliner formulation based on the combination of ciprofloxacin and chloramphenicol was successfully developed and comparatively evaluated. The best result was obtained with F4 formulation. The physical evaluation was suggestive of a cosmetically appealing and acceptable product with significant antimicrobial activity, revealing its importance towards health and protection of eyes against the eye infections like conjunctivitis and corneal ulcers. We can conclude that Netraliner shows synergistic effect.

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