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FORMULATION AND EVALUATION OF IBUPROFEN – LYCOPENE TRANS EMULGEL

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ABSTRACT

Lycopene is a carotenoid present in tomatoes. It occurs in the human diet predominantly in tomatoes and tomato products Lycopene is well absorbed if applied topically because it is fat soluble and has relatively small molecules. This pigment acts as an antioxidant in the body, protecting cells against damage from the free radicals formed when body cells burn oxygen for energy. The present study highlights the formulation and evaluation of Ibuprofen – *lycopene* emugel .The gel was prepared by using carbapol 934, gel base and the Ibuprofen drug was incorporated into the emulsion to produce transemulgel. The formulated transemulgel was evaluated for their rheological properties, drug content and diffusion studies. The transemugel has showed viscosity of 96cps**,** pH of 6.31 and good permeation capacity.

Key Words: Lycopene, transemugel, carbapol.

INTRODUCTION

Tomatoes are one of the most popular fruits on the planet. Although found in the vegetable section of your supermarket in botanical terms tomatoes are in fact a fruit grown from a vine. Tomatoes contain masses of vitamin C and are a rich source of vitamins A and B, as well as potassium, iron, phosphorus and fiber and huge amount of lycopene that tomatoes contain which has been associated with reduced risk of some cancers[1].

Lycopene is an antioxidant found in the cell walls of the tomato and is what makes them red it is part of the carotenoid family which are natural compounds that create the colours of fruits and vegetables. Dietary intake may not be sufficient to maximize skin benefits of lycopene. When ingested, lycopene is distributed throughout the entire body and only

relatively small amount finds its way into the skin[2]. Luckily, lycopene is well absorbed if applied topically (e.g. in a cream or lotion) because it is fat soluble and has relatively small molecules. The only possible downside of topical application is that lycopene may give your skin a bit of a tint (in the orange-red-bronze range). As an antioxidant, lycopene has been proven the most potent of all the carotenoid in quenching singlet oxygen[3].

A gel is a semisolid system of at least two interpenetrating phases: a gelling agent and a liquid .When gel and emulsion are used in combined form the dosage forms are referred as emu gel. Emu gels have emerged as one of the most interesting topical delivery system as it has dual release control system i.e. gel and emulsion. The major objective behind this formulation is delivery of hydrophobic drugs to systemic circulation via skin. In fact presence of a gelling agent in water phase converts a classical emulsion in to emu gel[4]. The emu gel for dermatological use has several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent & pleasing appearance.

Ibuprofen, an NSAID, commonly used for the relief of symptoms of arthritis, fever, primary dysmenorrheal and as an analgesic[5]. It also has an antiplatelet effect. This drug may infrequently cause serious bleeding from the stomach (or) intestine. This effect can occur without warning at any time while taking this drug. Older adults may be at higher risk for this effect. An improved Ibuprofen transemulgel formulation with a high degree of permeation could be useful in the treatment of locally inflamed skin and inflammatory and painful states[6].

Many of the dermal vehicles contain chemical enhancers and solvents to achieve these goals. But use of these chemical enhancers may be harmful, especially in chronic application, as many of them are irritants[7]. To improve the permeability of Ibuprofen, the use of gel bases is a logical approach to increase the drug flux across the epithelium. Emulgel helps in the incorporation of hydrophobic drugs into the oil phase and then oily globules are dispersed in aqueous phase resulting in o/w emulsion and this emulsion can be mixed into gel base. This may be proving better stability and release of drug than simply incorporating the drugs into gel base[8].

MATERIALS

Lycopene from tomatoes was selected on the basis of its anti-oxidant activity reported in the literatures. Ibuprofen is a gift sample from A-Z Laborataries, Chennai, India. All other chemicals were of analytical grade and used without further purification.

EQUIPMENTS

UV-Visible Spectrophotometer (Shimadzu), Diffusion apparatus (Franz diffusion cell), Magnetic stirrer (Remi Motors), P^H meter (Elico India).

METHODS

Extraction of Lycopene

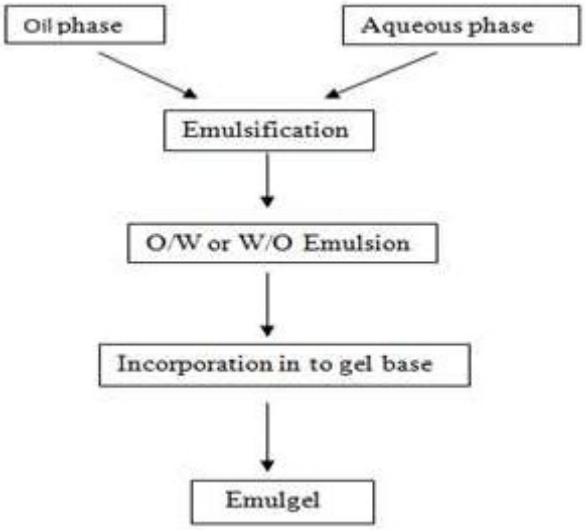
Lycopene extract from tomato is produced from a tomato variety with high lycopene content.The extract is produced by crushing tomatoes into crude tomato juice that is then separated into serum and pulp. The tomato pulp is then extracted with ethyl acetate. The final product is obtained after solvent removal by evaporation under vacuum at 40-60°C.

Preparation of lycopene gel

The lycopene extract obtained from tomatoes was treated with methanol to ensure dissolution completely ,then prepared 1% w/w carbapol 934 was added and dispersed uniformly until no lumps of carbapol is left. While dispersing the carbapol 0.5 %w/w Methyl paraben was added to the above mixture, as the carbapol gellifies under the alkaline conditions, Triethanolamine was added drop-wise until it forms the gel. The prepared *Lycopene* gel was weighed and stored in air tight containers in a dark room to prevent photo-oxidation.

Formulation of emulgel[9]

STEP1: Formulation of Emulsion either O/W or W/O
STEP2: Formulation of lycopene gel base
STEP3: Incorporation of emulsion into lycopene gel base with continuous stirring
The flow chart of emulgel preparation is shown in figure.



Flow chart of Emulgel formulation

Ibuprofen, one of the commonly used topical anti-inflammatory drug, is highly hydrophobic in nature was selected for preparation of Ibuprofen– *lycopene* transemulgel. Span 20 and liquid paraffin were used to prepare oil phase and 0.5 % w/w Ibuprofen was dissolved in oil phase. Tween 20 and purified water was used to prepare aqueous phase and 0.5 % methyl paraben was added to it by dissolving it in the propylene glycol. The oily phase and aqueous phase were heated separately at 70-80^0 C, oil phase is added to aqueous phase to produce o/w emulsion and then cooled to room temperature by continuous stirring. The prepared emulsion is incorporated in to gel base i.e lycopene gel produce emulgel.

EVALUATION OF GEL FORMULATION

RHEOLOGICAL EVALUATION[10-14]

Physical Observation

Transparency and Homogeneity

Viscosity

Viscosity of the prepared formulations was measured by using Brooke-field viscometer using spindle # 63 and the % torque for each formulation was as follows: 11.9 % torque for lycopene gel, 6.9% torque for Ibuprofen gel and 10.4 % torque for Ibuprofen -*lycopene* emulgel.

pH measurement

pH of the prepared formulation was carried out by using by digital pH meter.

Extrudability

The formulation was filled into collapsible metal tubes after the gel was set in the container. The extrudability of formulation was determined.

Spreadability

Two glass slides of standard dimensions were selected. The gel formulation whose spreadability had to be determined was placed over one of the slide. The other slide was placed on top of the gel in such a way that the gel was sandwiched between the two slides across a length of 6 cms along the slide.

Spreadability = M. L/T

M=wt tied to upper slide

L=length of glass slide

T=time taken in sec.

IN-VITRO EVALUATION

Drug content

1g of Ibuprofen - *Lycopene* transemulgel was weighed in 50 ml volumetric flask and the volume was made up to 50 ml using PBS-7.4. 1 ml of the solution was pipette out and made up to 10 ml using PBS-7.4. From this 1 ml of solution was pipette out and made up to 10 ml and the absorbance was measured at 273 nm using UV-Visible spectrophotometer. The same procedure was followed for the marketed Ibuprofen gel to estimate the drug content.

***In-vitro* diffusion studies**

The diffusion studies were performed using egg membrane as a barrier layer. 1g of the prepared Ibuprofen- *Lycopene* transemulgel was placed in the donor compartment. 100 ml of PBS-7.4 was taken as a medium in the acceptor compartment. The experimental setup is maintained under continuous stirring at room temperature. 5 ml of sample was withdrawn and filtered. 1ml sample filtrate was taken and diluted to 10 ml. From this 1 ml was pipette out and dilution to 10 ml. The samples were withdrawn for every 15 minutes for the first 1 hr (15, 30, 45 minutes and 1 hr) and 30 minutes interval for the next 2 hrs (1.5, 2.0, 2.5, 3.0 hrs). The samples were replaced with PBS-7.4 each time to maintain sink conditions. The same procedure was followed for marketed Ibuprofen gel omitting the last dilution.

RESULTS AND DISCUSSION

Calibration curve of Ibuprofen in phosphate buffer pH – 7.4

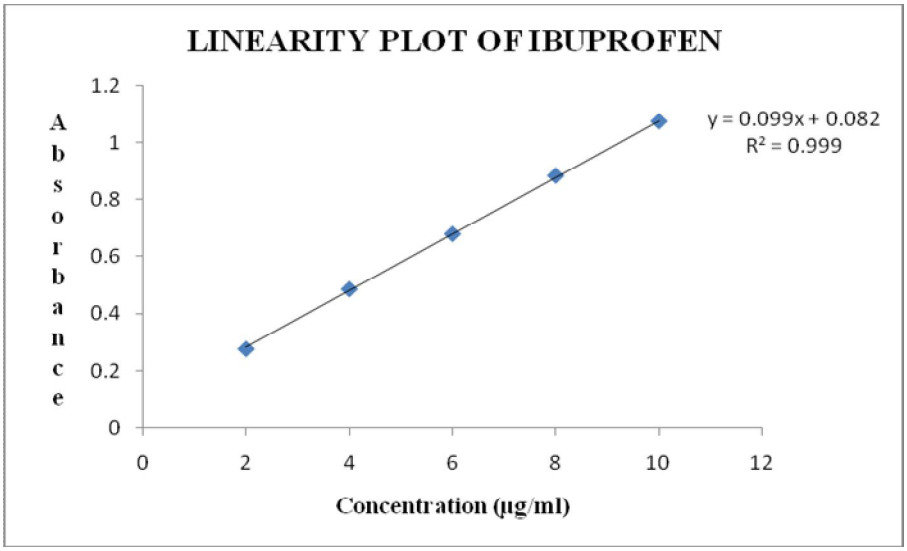
Preparation of Standard solution of Ibuprofen

100 mg of Ibuprofen drug was solubilised in methanol and the volume was made upto 100 ml using methanol: phosphate buffer pH-7.4 (PBS-7.4) in 1:1 volume ratios. From this solution 1 ml was pipette out and diluted to 10 ml using methanol: PBS-7.4 in 1:1 volume ratio to produce 100 µg/ml concentrations. From this 2, 4, 6, 8, 10µg/ml was prepared by dilutions and the absorbance was measured at 273 nm using UV-Visible spectrophotometer.

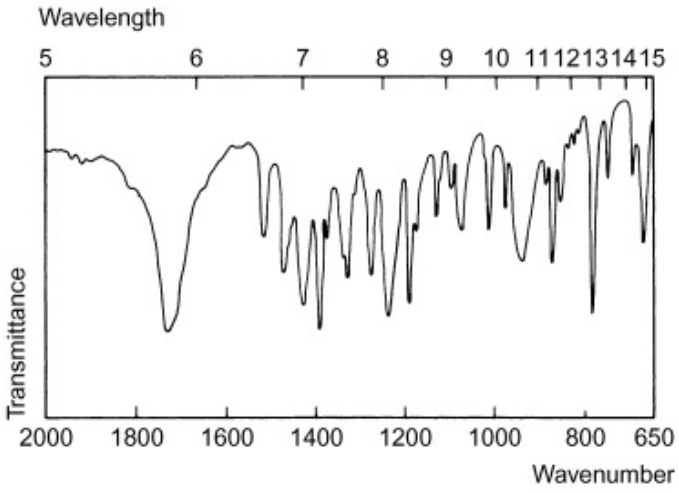
Calibration Curve Values Of Ibuprofen

S. No	Concentration (µg/ml)	Absorbance
1	2	0.277
2	4	0.486
3	6	0.679
4	8	0.883
5	10	1.073

Calibration curve of Ibuprofen in phosphate buffer ph – 7.4:



FT-IR OF IBUPROFEN



Preliminary evaluation of Ibuprofen– Lycopene emulgel

Percenatge yield of Lycopene gel

0.4g of lycopene extract was obtained from 250gm of tomatoes.30 g of Lycopene gel was obtained from 50 g of tomatoes. The % yield was found to be 61.35 % w/w.

Stability aspects of Lycopene gel and the Ibuprofen – Lycopene transemulgel

It was observed that the Lycopene formulations are highly unstable and highly susceptible to the microbial contamination. It may be due to the polysaccharide constituents present in the Lycopene. The formulations with methyl paraben as a preservative are comparatively more stable.

Viscosity

- Viscosity of Lycopene gel = 111 cps
- Viscosity of Lycopene emulgel = 60 cps
- Viscosity of Ibuprofen– Lycopene transemulgel = 96 cps

pH measurement

- pH of the Lycopene gel was found to be 5.1.
- pH of the Lycopene emulgel was found to be 5.92.
- pH of the Ibuprofen -Lycopene transemulgel was found to be 6.31.

Drug Content

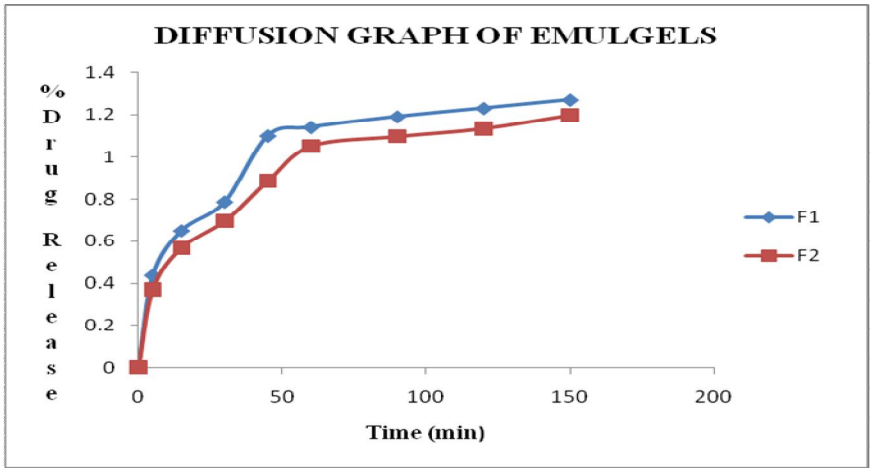
The absorbance was found to be 0.299 for Ibuprofen-*lycopene* emulgel at 273 nm using UV-Visible spectrophotometer. It was found to be 0.232 for Ibuprofen marketed gel.

S.NO	FORMULATION	DRUG CONTENT IN 100G OF FORMULATION
1	Ibuprofen- Lycopene transemulgel	72.4mg
2	Ibuprofen Marketed Gel	78.6mg

***In-vitro* diffusion studies: Diffusion profile of Ibuprofen-Lycopene transemulgel (F1) and Ibuprofen marketed gel (F2)**

S.No	Time (Min)	Absorbance		% Drug Release	
		F_1	F_2	F_1	F_2
1	5	0.156	0.132	0.436	0.370
2	15	0.236	0.216	0.650	0.568
3	30	0.329	0.254	0.787	0.697
4	45	0.383	0.365	1.100	0.886
5	60	0.410	0.385	1.140	1.053
6	90	0.424	0.401	1.190	1.098
7	120	0.435	0.417	1.230	1.135
8	150	0.455	0.436	1.270	1.198

***In-vitro* Diffusion Graph of Ibuprofen Emulgel (F1) and Marketed Emulgel(F2) in Phosphate Buffer Ph 7.4**



CONCLUSION

As the result of the experiment suitable medical form for the topical application of Ibuprofen-*Lycopene transemulgel* was developed. Performed examinations of prepared Ibuprofen-lycopene gel with tomato extract proved the significant antioxidant activity. The formulated gel was evaluated for visual appearance, pH, extrudability, Spreadability, drug content .And also lesser side effects can be expected from this formulation as the gel base is a natural ingredient. As the preparation containing the mixture of antioxidant substances in relatively low concentrations, this cream may be sufficient for the regular topical application as the effective long term protection of the skin against ROS caused damage.

REFERENCES

1. Agarwal S, Rao AV. Tomato lycopene and its role in human health and chronic diseases. *CMAJ* 2000; 163:739-744.
2. Porrini M, Riso P. Lymphocyte lycopene concentration and DNA protection fromoxidative damage is increased in women after a short period of tomato consumption. *J Nutr* 2000; 130:189-192.
3. Bohm F, Tinkler JH, Truscott TG. Carotenoids protect against cell membrane damage by the nitrogen dioxide radical. *Nat Med* 1995;1:98-99
4. Rao AV, Agarwal S. Role of antioxidant lycopene in cancer and heart disease. *J AmColl Nutr* 2000; 19:563-569.
5. Saravanan M, Dhanraju MD.The preparation,characterization and in-vitro release kinetics ofIbuprofen polystyrene Microspheres.Ind.J.PharmSci.2004; 66(3):287-292.
6. Saravanan M, Bhaskar K.Ibupropen loaded ethylcellulose /Polystyrene Micro spheres J.Microencapsulation.2003; 20(3):289-302.
7. Heber D, Lu QY. Overview of mechanisms of action of lycopene. *Exp Biol Med (Maywood)* 2002; 227:920-923.
8. Fuhrman B, Elis A, Aviram M. Hypocholesterolemic effect of lycopene and beta-caroteneis related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages. *Biochem Biophys Res Commun* 1997; 233:658-662.
9. Jacob SW, Francone CA, Lossow WJ.The Skeletal System. In: Structure and Function of Man, 3rd Edn, WB Saunders, Philadelphia: 106-148, (1982).
10. WB Saunders Co. Philadelphia, 1970, 55-60.

11. Ito Y, Suzuki K, Suzuki S, et al. Serum antioxidants and subsequent mortality rates of all causes or cancer among rural Japanese inhabitants. *Int J Vitam Nutr Res* 2002; 72:237-250.
12. John T, Rani S. Formulation and evaluation of gels of aqueous extract of centella Asiatic. Ind.J.Pharm.sci 1998;78.
13. Gupta M, Verma PRP, Marwaha RK, Faruk A, Singh G. Formulation and evalution of meloxicam gel. J.Pharm.research 2008;7:27-31.
14. Grimm W. Stability Testing of Drug Products Ind.Pharm 1982; 12:1259-92. Drug Stability guidelines. 4th rev, centre for veterinary medicines, FDA,US Dept of Health and Human Services,Washington,1990.