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Formulation and Evaluation of Methimazole-Loaded Emulgel for the Treatment of Melasma

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ABSTRACT

Melasma is a common acquired hyperpigmentation disorder characterized by the development of irregular, symmetrical, and brownish facial patches, which can significantly affect the appearance and quality of life of affected individuals. Methimazole, an antithyroid drug, has been investigated for its potential topical depigmenting activity due to its ability to interfere with melanogenesis. The present study was undertaken to develop and evaluate a methimazole-loaded emulgel intended for topical application in the management of melasma. Pre-formulation studies were carried out to determine the solubility, melting point, ultraviolet absorption maximum, and drug–excipient compatibility. The prepared formulations were evaluated for their physical appearance, homogeneity, pH, viscosity, spreadability, drug content, and in-vitro drug release characteristics. Drug–excipient compatibility was assessed using Fourier-transform infrared spectroscopy, while differential scanning calorimetry was employed to investigate the thermal characteristics of the formulation. The developed emulgels exhibited satisfactory physical characteristics with acceptable pH, viscosity, spreadability, and drug content, indicating their suitability for topical administration. In-vitro drug release studies demonstrated sustained release of methimazole from the emulgel formulations over the studied period. The release data were further analysed to understand the mechanism of drug release. Short-term stability studies were also performed to assess the physical and chemical stability of the prepared formulations. Overall, the study demonstrated the successful development of a methimazole-loaded emulgel with desirable physicochemical properties and controlled drug-release characteristics, suggesting its potential as a topical formulation for further investigation in the management of melasma. Emulgel have several merits like greaseless, easily spreadable, easily removable, emollient and transparency.

Keywords: Topical drug delivery system, Methimazole, Emulgel, *In vitro* diffusion studies.

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INTRODUCTION

Melasma is a common, chronic, and cosmetically distressing hyper pigmented disorder of the skin, characterized by symmetric, irregular, light-to-dark brown macules and patches predominantly localised on the malar eminences, forehead, nose, upper lip, and chin ^[1]. Melasma is the overproduction of melanin in the skin and came from the Greek translate of phrase black (melas). Melasma is one of the most popular, therapy- resistance types of acquired hyperpigmentation. The risk of melasma infection in females is nine times more than males, and it is more often in darker- skinned individuals, such as Hispanics, Asians, or other racial groups ^[2].

Emulgel are oil-in-water or water in oil emulsions that are gelled by mixing with a gelling agent. Emulsifying gels are excellent stable vehicles for hydrophobic or poorly water-soluble drugs. In simple terms, the emulsion is a combination of emulsion and gel. Emulgel is manufactured as both an oil-in-water and water-in-oil emulsion mixed with a gel. Oil-in-water is used for lipophilic drugs and water-in-oil is used for hydrophobic drug delivery. Emulgel is more effective in curative aspects than regular gel ^[3].

Melasma is a chronic acquired hyperpigmentation disorder characterized by excessive melanin production. Methimazole has emerged as a promising topical pigmented agent because it inhibits melanogenesis by acting as a peroxidase inhibitor and suppressing tyrosinase- mediated melanin synthesis. Unlike hydroquinone, methimazole does not exert cytotoxic effects on melanocytes, making it a safer alternative for prolonged use.^[4] The pathophysiology of melasma remains elusive, but multiple factors have been implicated. The role of female hormonal activity has been suggested by the increased frequency of occurrence of melasma in pregnancy and in those on oral contraceptive pills, estrogen replacement therapy, and estrogen treatment for prostatic cancer.^[5]

Other various advantages of emulgel include easy incorporation of drugs, augmented drug loading capacity, production feasibility (simple and short processing steps) and low preparation cost, avoidance of first-pass metabolism and gastrointestinal incompatibility, improved patient compliance, suitability for self-medication, narrow therapeutic window and selective to a specific site.^[6]

Methimazole an antithyroid drug, it is available as conventional tablet dosage form in market of 5mg, 10mg and 20mg. which is prescribed to be taken 3-4 times a day with usual treatment period of 16-18 weeks. It was chosen as a drug model for the present research work because it full fills all the criteria needed for a successful transdermal dosage form to deliver the drug to a patient in effectively and safely and to overcome the limitation of oral methimazole treatment by eliminating

multiple doses with single sustained released patch, by pass first pass metabolism, gastro irritability and with better patient compliance [7].

MATERIALS AND METHOD

Materials

- Methimazole
- Carbopol 934
- Carbopol 940
- Liquid paraffin
- Tween 20
- Span 20
- Propylene glycol
- Ethanol
- Methyl paraben
- Propyl paraben
- Triethanolamine
- Purified water

Equipment's

- Weighing balance
- Magnetic Stirrer
- Water Bath
- Beakers
- Measuring Cylinders
- Brookfield Viscometer
- UV

Method

1. Preparation of Aqueous phase

Aqueous phase of emulsion was prepared by dissolving tween 20 in distilled water.

2. Preparation of Oil phase

Span 20 dissolved in liquid paraffin. Methyl paraben and Propyl paraben were dissolved in propylene glycol. Drugs were dissolved in ethanol, and both solutions were mixed with the aqueous phase. Both the oil and aqueous phases were heated separately to 75⁰c, and the oil phase was added to the water phase with continuous stirring until cooled.

3. Emulsification

The aqueous phase and oil phase were separately heated to 70°C and then oil phase was slowly added to aqueous phase using homogenizer with continuous stirring at 1000rpm till emulsion is obtained.

4. Formulation of gel base

In a beaker 25 ml water was taken and calculated quantity of Carbopol 930 was added and stirred on a magnetic stirrer at 600 rpm till a firm gel was obtained. Similarly, Carbopol 940 gel was prepared. In another beaker 25 ml water was taken and calculated quantity of HPMC 15cps was added and stirred on a magnetic stirrer at 600 rpm and later stored for overnight to get a firm gel was obtained.

5. Preparation of Methimazole topical transemul gel

The prepared emulsions were mixed dropwise with respective gel base separately with continuous stirring on a magnetic stirrer at 600 rpm to obtain the emulgel and pH was adjusted by using 0.1 ml of triethanolamine. The prepared emulgels were packed in wide-mouth glass jar covered with secure capped plastic lid. The resulting emulsion was mixed with the gel under gentle stirring to obtain an emulgel^[3].

PRE-FORMULATION STUDIES

Physical appearance

Organoleptic properties were observed.

Solubility study

Qualitative solubility of methimazole in various solvents was measured using NF, 2007. Approximately 1 mg of Methimazole was weighed and transferred into a 10 ml test tube and dissolved in the respective solvents (1 ml each of methanol, ethanol, PBS solution, and water).

Melting point

Melting point determination of the pure drug was done, as it is a first point indication of purity of sample. Melting point of drug methimazole was determined by capillary fusion method using a melting point apparatus. Melting point was recorded and compared with literature value.

Preparation of Calibration curve

Accurately 100 mg of Methimazole was weighed and was dissolved in 100 ml of pH 7.4 phosphate buffer to give a 1 mg/ml. which gave the 1st stock solution. From the 1st stock solution 2 ml was pipetted and transferred to 100 ml volumetric flask and volume was made up with pH 7.4 phosphate buffer up to 100 ml to give 20 µg/ml, 2nd stock solution.

Aliquots 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5 ml from 2nd stock solution and diluted up to 10 ml with pH 7.4 phosphate buffer to give 1 to 10 µg/ml respectively. The sample solution were then scanned at UV spectrophotometer at 252 nm and absorbance were recorded, and graph was plotted between absorbance and concentration to obtain a calibration curve.

Preparation of Phosphate Buffer pH 7.4

- 0.2 m potassium dihydrogen phosphate (KH₂PO₄): Weigh 27.218 g of KH₂PO₄, dissolve in distilled water, and make volume up to 1000 ml in a volumetric flask.
- 0.2 m sodium hydroxide (NaOH): weigh 8.00g of NaOH, dissolve in distilled water, and make volume up to 1000 ml.
- To prepare pH 7.4 buffer, 250 ml of KH₂PO₄ solution was mixed with 195.5 ml of NaOH solution and diluted to 1000 ml with distilled water. The pH was checked and adjusted to 7.4

Preparation of standard graph

From stock solutions of Methimazole (100mg/100ml) prepared in distilled water and phosphate buffer pH 7.4 serial dilutions of 50-500 µg/ml were made. The absorbance of each dilution was measured spectrophotometrically at λ max, using the respective medium as blank. A calibration graph (absorbance vs concentration) was plotted, and linear regression analysis was performed to derive the equation for concentration estimation [6].

Fourier transmission Infra-Red Spectroscopy [FTIR]

A compatibility check was carried out between the ingredients through FT-IR studies. FTIR studies were performed on pure drug methimazole and the study was carried out for each individual ingredient, such as Carbopol 940 & 934. And also carried out for emulgel formulation F5 and formulation F9. The FT-IR spectra support the identification of the functional groups present in the compound. The FTIR spectra were used in comparing the formulation spectra with a standard FTIR spectrum of the pure drug to detect any physicochemical incompatibility between the drug and different excipients.

CHARACTERIZATION OF METHIMAZOLE EMULGEL

Visual Examination

The prepared emulsions were observed for microscopic images of emulsion, colour, homogeneity, consistency and phase separation.

Drug content

The drug content of Methimazole emulgel was determined to assess the uniformity of drug distribution within the formulation. A known quantity of gel (1g) was accurately weighed and

transferred into a 100 ml volumetric flask containing a suitable solvent such as phosphate buffer pH 7.4, followed by sonication for 30 minutes to ensure complete extraction of the drug.

The resulting solution was filtered through Whatman filter paper No.1 to remove any polymeric residues, and appropriate dilutions were made with the same buffer. The absorbance of the final solution was measured using a UV- visible spectrophotometer at 295 nm against a blank. The drug content was calculated with reference to a previously constructed calibration curve of methimazole in phosphate buffer pH 7.4. According to USP, drug content is satisfactory if 85% - 115 % of drug is detected in the emulgel formulations [7].

Determination of pH

The pH of the methimazole emulgel was measured using a digital pH meter (Digisum electronics, Hyderabad). The measurement of pH was carried out in triplicate.

Entrapment Efficacy (%)

A known quantity of the prepared emulgel formulation was accurately weighed and dispersed in a suitable volume of phosphate buffer pH 7.4. The dispersion was subjected to centrifugation to separate the entrapped drug from the untrapped/free drug. After centrifugation, the supernatant containing the free drug was carefully separated. The supernatant was suitably diluted with phosphate buffer pH 7.4 and its absorbance was measured using a UV–Visible spectrophotometer at 252 nm. The concentration of untrapped methimazole was determined from the previously prepared calibration curve. The amount of entrapped drug was calculated by subtracting the amount of free drug from the total drug initially added [11,12].

$$\% \text{ EE} = \frac{\text{Total Mass of Dapsone Added} - \text{Mass of Free Dapsone in}}{\text{Total Mass of Dapsone Added}}$$

Spreadability

Spreadability of the prepared emulgel formulations was determined by the slip-and-drag method using two glass slides. About 1 g of emulgel was placed uniformly between two glass slides of similar dimensions. The slides were pressed gently to obtain a uniform layer and to remove any entrapped air. Excess emulgel adhering to the edges of the slides was carefully removed. The lower slide was fixed firmly, while the upper slide was connected to a thread passing over a pulley. A known weight was attached to the thread, and the time required for the upper slide to move through a fixed distance was recorded. The Spreadability was calculated using the equation

$$S = M \times L/T,$$

where M is the applied weight, L is the distance travelled, and T is the time taken. The test was performed in triplicate, and the mean spreadability value was reported in g·cm/sec; a shorter time

indicated better spreading ability^[13].

Viscosity

The viscosity of the prepared emulgel formulations was determined using a Brookfield viscometer. A suitable spindle was selected according to the consistency of the formulation. Approximately 50 g of emulgel was transferred into a clean, dry beaker. The sample was allowed to equilibrate at room temperature before measurement. The spindle was immersed carefully into the emulgel without introducing air bubbles. The viscosity was measured at a predetermined rotational speed of the spindle. The reading was allowed to stabilize, and the viscosity was recorded in centipoise (cP). The measurement was performed in triplicate, and the mean $\pm$ standard deviation was calculated^[14].

Washability

A small quantity of the prepared emulgel was uniformly applied onto the skin surface and allowed to remain for a short period. The applied formulation was then washed gently with sufficient quantity of water using light rubbing. The ease of removal of the formulation from the skin was visually assessed. The formulation was considered washable when it was removed completely without leaving a noticeable greasy or sticky residue. The observations were recorded qualitatively for each formulation^[15].

Extrudability

The extrudability of the prepared emulgel formulations was evaluated using a collapsible aluminum tube. A predetermined quantity of emulgel was filled into the tube and the tube was sealed properly. The formulation was extruded by applying a known weight to the tube. The weight required to extrude a continuous ribbon of approximately 0.5 cm length within 10 seconds was recorded. The test was carried out separately for each formulation under identical experimental conditions. Each measurement was performed in triplicate and the mean value was calculated^[16].

$$\text{Extrudability} = \text{Applied weight (g)} / \text{Area (cm}^2\text{)}.$$

Determination of pH

The pH of the prepared emulgel formulations was determined using a calibrated digital pH meter. About 1 g of emulgel was dispersed in 100 mL of distilled water and allowed to equilibrate for approximately 2 h at room temperature. The pH meter was calibrated using suitable standard buffer solutions before measurement. The electrode was immersed in the prepared emulgel dispersion, and the pH was recorded after stabilization. The measurement was performed in triplicate, and the results were expressed as mean $\pm$ standard deviation (SD)^[17,18]

***In-vitro* diffusion study**

Preparation of cellophane membrane for the diffusion studies

The cellophane membrane approximately 25 cm × 2 cm was taken and washed in the running water. It was then soaked in distilled water for 24 hours, before used for diffusion studies to remove glycerin present on it and was mounted on the diffusion cell for further studies.

Diffusion studies

The *in-vitro* diffusion of drug from the different gel preparations were studied using the classical standard cylindrical tube fabricated in the laboratory; a simple modification of the cell is a glass tube. The diffusion cell membrane was applied with one gram of the formulation and was tied securely to one end of the tube, the other end kept open to ambient conditions which acted as donor compartment. The cell was inverted and immersed slightly in 250 ml of beaker containing neutralizing buffer, freshly prepared (pH 7.4) as a receptor base and the system was maintained for 2 hrs at 37±0.2°C. The media was stirred using magnetic stirrer. Aliquots, each of 5 ml volume were withdrawn periodically at predetermined time interval of up to 12 hrs and replaced by an equal volume of the receptor medium. The aliquots were suitably diluted with the receptor medium and analyzed by UV-visible spectrophotometer at 252 nm using neutralizing phthalate buffer as blank [8].

RESULTS AND DISCUSSION

Table 1: Physical Properties

Formulation	Observation	Washability	Extrudability
F1	White creamy	++	+++
F2	White creamy	+++	+++
F3	White creamy	+++	++
F4	White creamy	++	+++
F5	White creamy	+++	+++
F6	White creamy	+++	+++
F7	White creamy	++	++
F8	White creamy	+++	+++
F9	White creamy	+++	+++
F10	White creamy	+++	+++
F11	White creamy	+++	++
F12	White creamy	++	+++

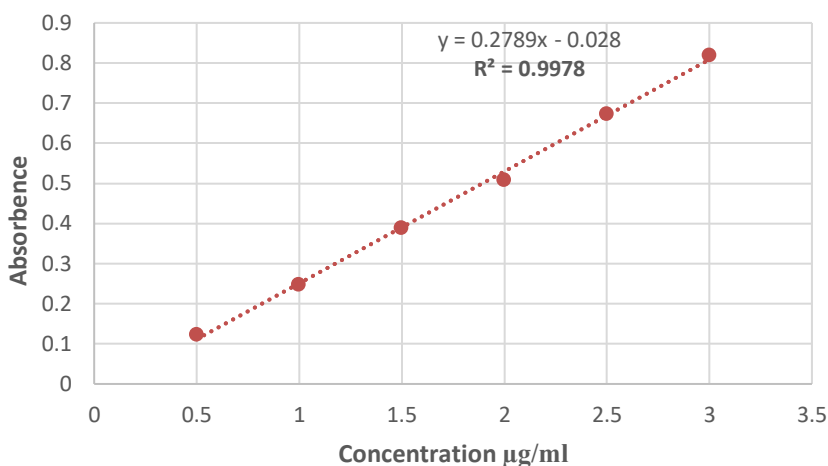
Excellent: +++, Good: ++

The prepared methimazole emulgel formulations when subjected for color appearance were white creamy with a smooth homogenous texture and glossy appearance.

Construction of standard calibration curve in pH 7.4 by UV – Visible spectroscopy

Table 2: Calibration curve of Methimazole in pH 7.4 buffer solution

Sr.No	Concentration (µg/ml)	Absorbance at 252nm
1	0.5	0.1237
2	1	0.2484
3	1.5	0.3885
4	2	0.5089
5	2.5	0.6734
6	3	0.8206

**Figure 1: Calibration Curve of Methimazole in pH 7.4 buffer solution**

The calibration curve of methimazole was constructed in phosphate buffer (pH 7.4) using a UV–Visible spectrophotometric method at its determined absorption maximum (λ_{max}) of 252 nm. The calibration plot of absorbance versus concentration exhibited excellent linearity over the selected concentration range, with a correlation coefficient (R^2) of 0.9978. This high R^2 value indicates a strong linear relationship between concentration and absorbance.

Drug – excipients compatibility study by using FTIR

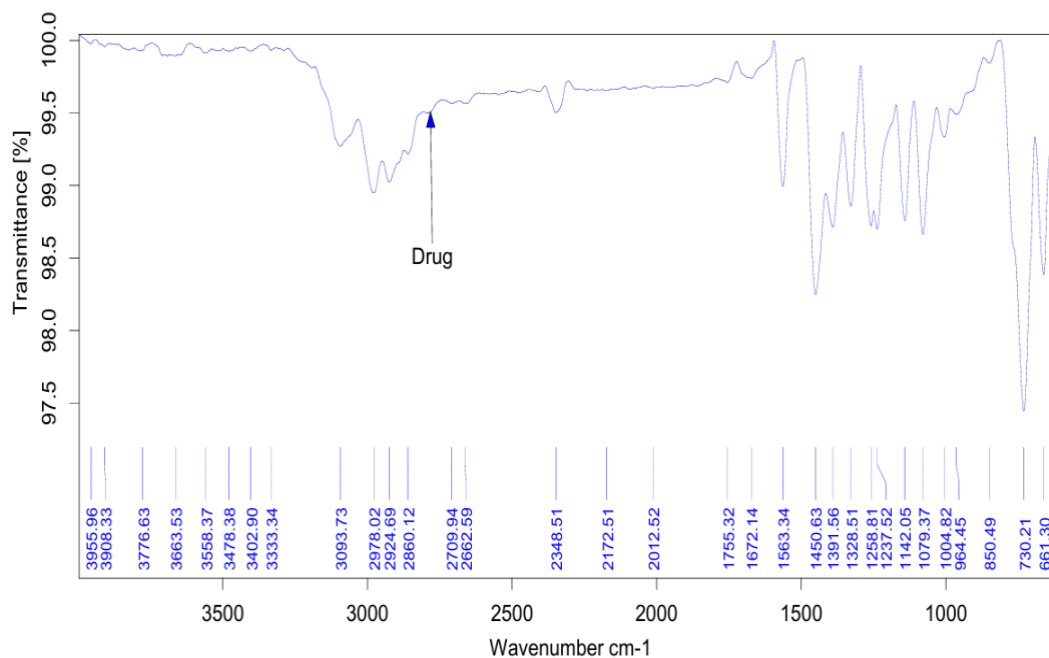


Figure 2: FTIR spectrum of pure Methimazole

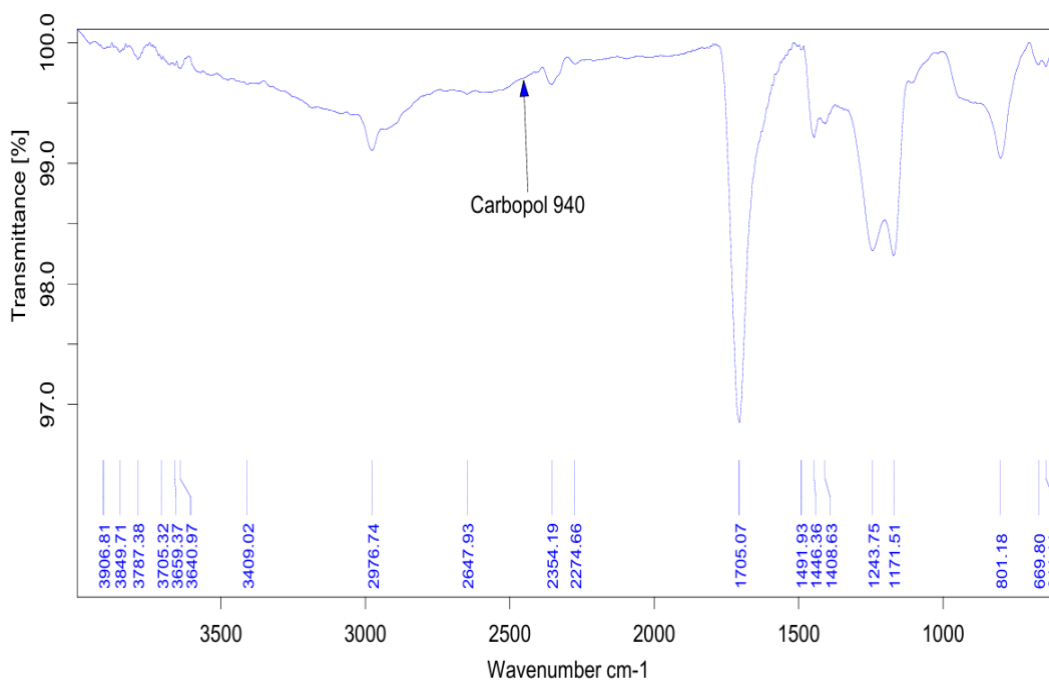


Figure 3: FTIR spectrum of Carbopol 940

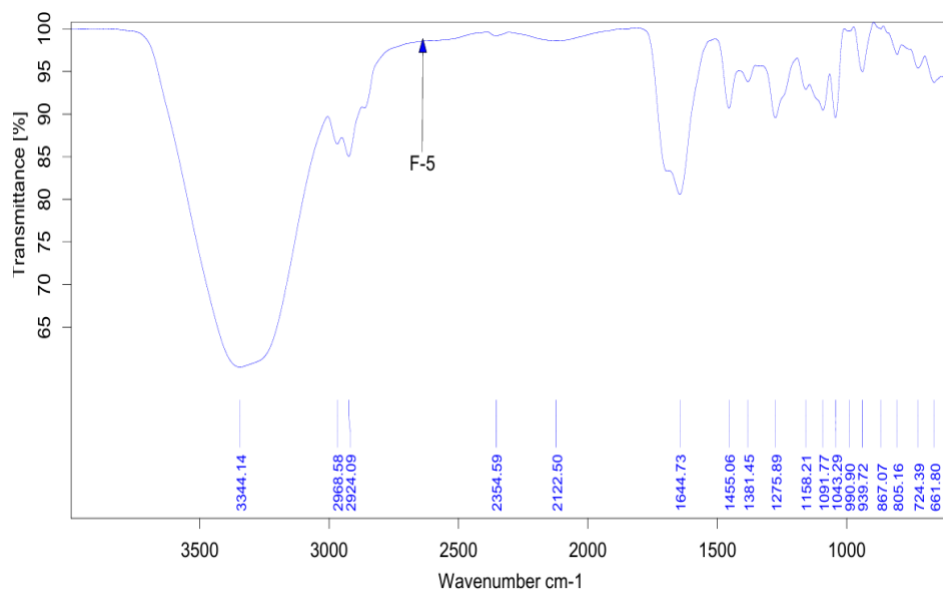


Figure 4: FTIR spectrum of F5

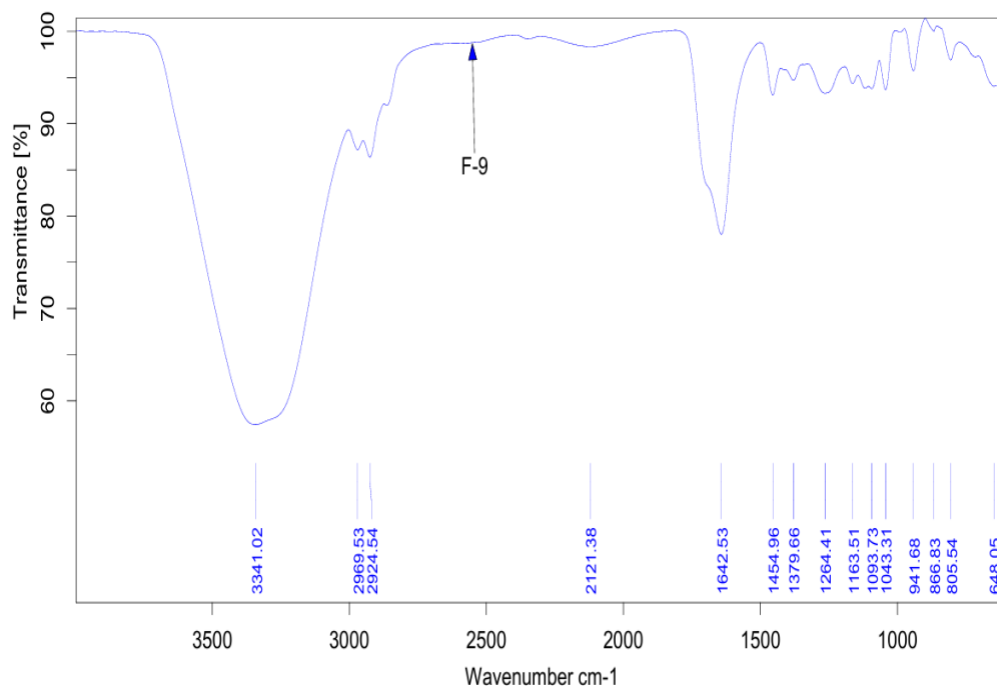


Figure 5: FTIR spectrum of F9

Table 3: Characteristic IR Absorption Bands of Methimazole, Carbopol 940, F5 & F9

SI. No	Name of the compound	Functional Groups	Mode of Vibrations	Wavenumber (cm-1)
1	Methimazole	N-H stretching	Secondary amine	3093.73
		C-H stretching (Aliphatic)	Methyl group	2978.02, 2924.69, 2860.12
		C=C stretching	Heterocyclic ring	1563.34
		C-N stretching	Imidazole ring	1328.51, 1258.81, 1142.05
		C-S stretching	Sulfur containing ring	730.21, 661.30
2	Carbopol 940	O-H stretching	Hydrogen-bonded carboxylic acid	3906.81, 3849.71, 3659.37, 3640.97,

3	F5	C-H stretching (Aliphatic)	Aliphatic –CH ₂ group	2976.74
		O=C=O stretching	Atmospheric CO ₂	2354.19, 2274.66
		C=O stretching	Carboxylic acid	1705.07
		CH ₂ bending	Aliphatic polymer	1491.93, 1446.36,
		O-H stretching	Hydrogen-bonded hydroxy group	3344.14
		C-H stretching	Methyl (–CH ₃) group	2968.58, 2924.09
		CH ₃ bending	Methyl group	1455.06, 1381.45
		C–N stretching	Imidazole ring	1275.89, 1158.21
		C=S stretching	Thioamide group	1091.77, 1043.29
		C–N/C–S stretching	Heterocyclic ring	990.90, 939.72
4	F9	C–S stretching	Sulfur-containing ring	724.39, 661.80
		O-H stretching	Hydrogen-bonded hydroxyl group	3341.02
		C-H stretching	Methyl (–CH ₃) group	2969.53, 2924.54
		C=N stretching	Imidazole ring	1642.53
		CH ₃ bending	Methyl group	1454.96, 1379.66
		C–N stretching	Imidazole ring	1264.41, 1163.51
		C=S stretching	Thioamide group	1093.73, 1043.31
		C–N/C–S stretching	Heterocyclic ring	941.68, 866.83
		C–S stretching	Sulfur-containing ring	805.54, 648.05

The FTIR spectrum of pure methimazole showed characteristic peaks at 2978, 1672, 1451, 1238, and 1045 cm⁻¹, confirming the presence of its functional groups and the purity of the drug. Similarly, Carbopol 934 and Carbopol 940 exhibited their characteristic absorption peaks corresponding to their polymeric structure. The FTIR spectra of formulations F5 and F9 showed all the major characteristic peaks of methimazole with only minor shifts in their positions. No new peaks were observed, and none of the characteristic peaks of methimazole disappeared, indicating the absence of any significant chemical interaction between the drug and the excipients.

Table 4: Drug content of Methimazole emulgel

Sl.NO	Formulation code	Drug Content (%)
1	F1	90.24 ± 0.42
2	F2	95.18 ± 0.28
3	F3	93.76 ± 0.39
4	F4	96.42 ± 0.26
5	F5	97.56 ± 0.29
6	F6	92.05 ± 0.51
7	F7	94.52 ± 0.31
8	F8	97.08 ± 0.33
9	F9	99.14 ± 0.25

10	F10	95.94 ± 0.35
11	F11	97.92±0.24
12	F12	97.98±0.23

The drug content study of the prepared Methimazole emulgel formulations (F1–F12) showed satisfactory drug incorporation in all batches. The drug content values ranged from $90.24 \pm 0.42\%$ to $99.14 \pm 0.25\%$, indicating uniform distribution of Methimazole throughout the emulgel formulations. Among all the formulations, F9 showed the highest drug content ($99.14 \pm 0.25\%$), However, all formulations showed acceptable drug content with low standard deviation values, indicating good uniformity and reproducibility. Therefore, the developed Methimazole emulgels are considered suitable for further evaluation such as in vitro drug release, stability, and other pharmaceutical studies.

Table 5: pH of Methimazole emulgel

SI.NO	Formulation code	pH (±S.D.)
1	F1	6.01 ± 0.03
2	F2	5.89 ± 0.04
3	F3	5.82 ± 0.03
4	F4	6.08 ± 0.04
5	F5	6.24 ± 0.03
6	F6	6.18 ± 0.02
7	F7	6.35 ± 0.03
8	F8	5.94 ± 0.02
9	F9	6.47 ± 0.03
10	F10	5.92 ± 0.02
11	F11	6.35 ± 0.03
12	F12	6.41 ± 0.02

The pH of all prepared Methimazole emulgel formulations (F1–F12) was evaluated to determine their suitability for topical application. The observed pH values ranged from 5.82 ± 0.03 to 6.47 ± 0.03 , indicating that all formulations were within the acceptable pH range for skin application. Formulation F9 showed the highest pH (6.47 ± 0.03). The slight variation in pH among the formulations may be attributed to differences in the concentration of gelling agents, emulsifying agents, and other excipients used during formulation.

Table 6: Viscosity of Methimazole emulgel

SI.NO	Formulation code	Viscosity (cps)
1	F1	2070 ± 16
2	F2	1985 ± 14
3	F3	2230 ± 17
4	F4	1825 ± 12
5	F5	2155 ± 18
6	F6	1910 ± 15

7	F7	2315 ± 19
8	F8	2570 ± 22
9	F9	2790 ± 25
10	F10	2680 ± 24
11	F11	2485 ± 21
12	F12	2400 ± 20

Viscosity is one of the most important parameters in the evaluation of topical emulgels. The viscosity of the prepared Methimazole emulgel formulations (F1–F12) was found to be range from 1825 ± 12 cps to 2790 ± 25 cps. Among all the formulations, F9 showed the highest viscosity (2790 ± 25 cps). The viscosity values obtained were within an acceptable range for topical application, Overall, the viscosity study confirmed that the prepared emulgels possessed appropriate rheological characteristics for effective topical application.

Table 7: Spreadability of Methimazole emulgel

SI.NO	Formulation code	Spreadability (g.cm/sec)(±S.D.)
1	F1	6.95 ± 0.12
2	F2	7.36 ± 0.16
3	F3	7.82 ± 0.13
4	F4	6.48 ± 0.14
5	F5	8.24 ± 0.15
6	F6	8.71 ± 0.12
7	F7	10.08 ± 0.13
8	F8	9.15 ± 0.14
9	F9	10.91 ± 0.12
10	F10	6.12 ± 0.11
11	F11	9.62 ± 0.11
12	F12	10.54 ± 0.15

The spreadability of the prepared Methimazole emulgel formulations (F1–F12) was evaluated to determine the ease of application on the skin. The spreadability values ranged from 6.12 ± 0.11 to 10.91 ± 0.12 g.cm/sec, An ideal topical emulgel should possess good spreadability to ensure patient convenience and effective drug distribution. Among all the formulations, F9 exhibited the highest spreadability (10.91 ± 0.12 g.cm/sec), followed by F12 and F7. Based on its excellent spreading ability along with satisfactory physicochemical characteristics, F9 was selected as the optimized formulation, as it offers easy application, uniform drug distribution, and improved patient acceptability for topical Methimazole delivery.

In vitro drug release studies

Table 8: In vitro release data of pure drug Methimazole

Time (mins)	Dissolution Medium	% CDR
0	Phosphate buffer	0
5	pH 7.4	18.3
10		27.2
15		31.54
30		44.3
60		61.14
120		72.15
180		74.3
240		90.38

An *in vitro* study on drug release was conducted for Pure Drug (Methimazole) utilizing 900ml of a pH 7.4 phosphate buffer solution, as well as 900ml of a 0.1% pH 7.4 phosphate buffer solution, to determine the cumulative percentage of drug release(%CDR).

Table 9: In vitro release data of different formulations (F1 to F7)

Time (mins)	Dissolution Medium	% CDR						
		F1	F2	F3	F4	F5	F6	F7
0	Phosphate buffer	0	0	0	0	0	0	0
15	pH 7.4	9.8	12.3	12.06	10.82	10.3	13.6	13.5
30		15.5	18.9	21.36	19.42	26.1	22.4	23.24
60		27	30.4	34.28	31.42	34.06	35.2	37.18
120		40.8	43.2	46.72	43.18	47.04	46.8	51.26
180		50.2	52	57.36	53.48	57.82	59.6	62.18
240		59.3	58.5	65.38	61.24	66.18	64.7	69.05
300		64.2	63.4	71.84	67.36	72.54	74.46	71.65
360		68.82	68.7	76.84	72.18	77.46	79.82	75.36
420		72.84	72.8	80.94	76.48	81.82	83.96	79.64
480		76.18	77.8	84.16	79.62	85.34	87.62	84.72
540		78.24	84.18	86.92	82.46	88.12	90.48	87.36
600		81.42	87.24	89.68	85.38	91.26	93.42	89.84

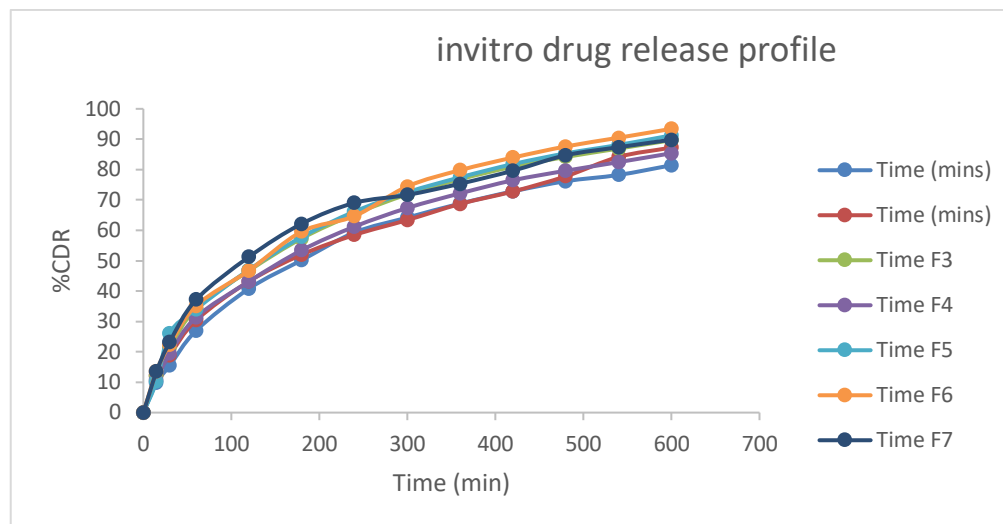


Figure 6: *In Vitro* release profile of Methimazole loaded Emulgel (F1 – F7).

Table 10: *In vitro* release data of different formulations (F8 to F12)

Time (mins)	Dissolution Medium	% CDR				
		F8	F9	F10	F11	F12
0	Phosphate	0	0	0	0	0
15	buffer pH 7.4	12.84	14.26	11.92	13.48	13.76
30		22.65	25.18	21.34	23.76	24.12
60		34.82	38.46	33.25	36.58	37.24
120		48.36	53.72	46.84	50.65	51.42
180		58.74	64.85	56.92	61.38	62.24
240		66.52	73.46	64.38	69.72	70.58
300		72.84	79.35	70.26	75.68	76.82
360		77.96	84.62	75.48	81.54	82.36
420		81.84	88.56	79.62	85.48	86.54
480		84.96	91.42	82.86	88.34	89.62
540		87.38	93.64	85.48	90.72	91.84
600		89.26	95.18	87.42	92.64	93.56

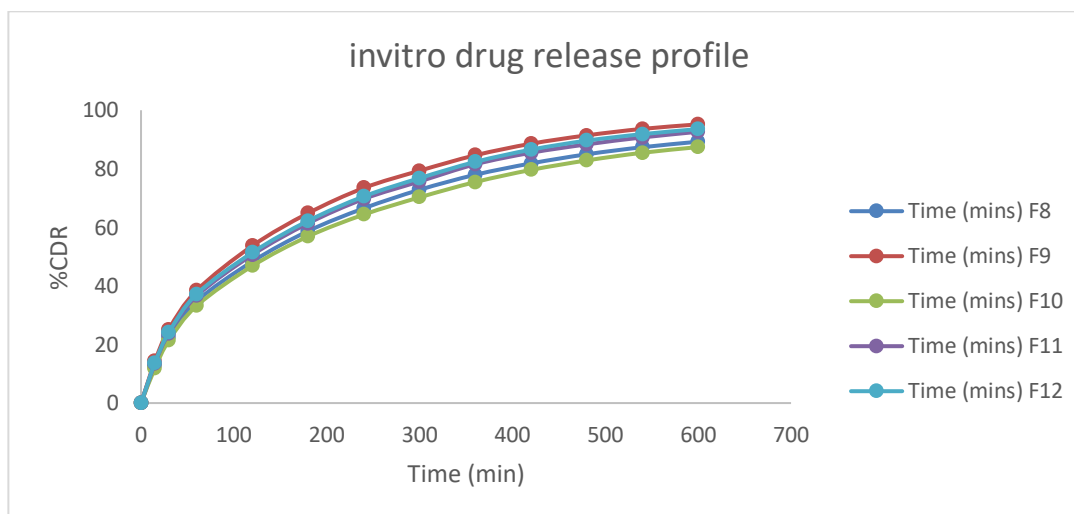


Figure 7: *In Vitro* release profile of Methimazole loaded emulgel (F8 – F12)

The *in-vitro* drug release study was carried out on all formulations by suspending the methimazole loaded emulgel in a pH 7.4 phosphate buffer solution, determining the cumulative percentage drug release of Methimazole-loaded Emulgel over a duration of 10 hours. The Methimazole topical emulgel F9 prepared with Carbopol 940 was selected as the optimum formulation due to its high drug release and comparatively higher yield. Effect of polymer type and drug: polymer ratio on the drug release pattern of formulated methimazole emulgels was studied.

Table 11: Percentage drug entrapment efficiency (%EE)

Formulation code	Entrapment efficiency (%EE)
F1	85.42%
F2	90.6%
F3	89.92%
F4	87.12%
F5	90.60%
F6	86.11%
F7	91.68%
F8	86.40%
F9	93.30%
F10	92.2%
F11	85.42%
F12	91.90%

Drug entrapment efficiency of all the formulations were evaluated by dissolving Methimazole loaded emulgel in methanol and analyzed for Methimazole content by using UV-spectroscopy at 252nm. The entrapment efficiency results ranged between 85.42 to 93.30%

CONCLUSION

Pre-formulating studies of Methimazole were carried out, and the results were in agreement with reported pharmacopoeial and literature standards. FTIR compatibility studies showed no significant interaction between Methimazole and the selected excipients, indicating good drug-excipient compatibility. All formulations demonstrated acceptable viscosity and spreadability, ensuring easy application and good patient compliance. The drug content of Methimazole emulgel was found in the range of 90-99% confirming uniform distribution and entrapment of drug. The pH of all formulations was in the range compatible with the normal pH range of the skin. The viscosity of all formulations was found to be within the acceptable range for topical emulgels, indicating appropriate consistency and stability. The obtained spreadability values suggest that the developed emulgels possess good patient acceptability and are suitable for topical drug delivery. In-vitro drug release studies showed sustained and controlled release of Methimazole from the emulgel formulations. Among all the prepared formulations, F9 exhibited the best overall

performance based on physicochemical characteristics, drug content, spreadability, viscosity, and drug release profile.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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