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FACTORS AFFECTING THE FORMULATION FOR THE STABILIZATION OF SECNIDAZOLE IN GEL PREPARATIONS

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ABSTRACT

Secnidazole gels (G1-G10) were prepared byhydroxypropyl methylcellulose at different concentrations (2.5-7.5%) and glycerin and propylene glycol were used as humectants which may affect the rheological properties of SEC gels. The viscosities of SEC gels were 3100-5300 centipoise. Different formulations of SEC gels were packed and subjected to accelerated stability studies at 40±2°C/75%±5% relative humidity for 6 months. Due to the stability of SEC against dry heat and hydrolytic degradation, the degradation rate of SEC gels in different formulation of glycerin and propylene glycol was 6.29-8.11% and 7.52-9.57%, respectively. The kinetics of SEC photolysis was also investigated using UV-visible spectrophotometer. The absorption spectra of SEC and its photolyzed product showed its peak (λ_{max}) at 318 and 209nm, respectively, with an isosbestic point at ~295 nm. The values of first-order rate constants (k_{obs}) of SEC in gels were 3.92-6.03×10^{-2} min^{-1}, compared to 11.81×10^{-2} min^{-1} in aqueous solution. A linear relation was observed between the k_{obs} of SEC mainly with an increase in the concentration of HPMC, GL, and PG in gels with a negative slope. The shelf-life of photolyzed SEC in the gels increased to ~3.0 fold. Since there is no chemical interaction between SEC and excipients used in formulations, the stability of SEC gels is mainly due to the increased viscosity by decreasing oxygen penetration. Thus, the chances of oxidation and photo-oxidation degradation were minimized. It is suggested that such an approach may be useful in the stabilization of photo-labile drugs in viscous formulations.

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Introduction

Topical gels are applied to the skin or mucosal membrane to obtain the local effect of the drug, directly at the site of action for an extended time with minimum side effects [1]. Gels enhance patient's compliance due to their non-invasive technique, lesser side effects, and minimum drug-food interactions [2]. They are not affected by gastrointestinal or liver enzymes as they do not pass through pre-systemic elimination in the gastrointestinal tract [3-7]. The gels have an interlinked matrix system. The gelling agents are uniformly distributed in the liquid phase [8]. They are diluted and transit linked polymeric matrix networks that exhibit solid (non-liquid) colloidal networks at a steady-state [9]. The swelling property of the gelling agents is one of the most important formulation considerations for the preparation of gels [10]. Gels must be non-greasy and dignified in the state [11]. They must have a good adherence property, good retention ability, with good spreadability property.

Secnidazole (SEC) (anti-infective) **(Figure 1)** is belonging to nitroimidazole. It is chemically known as (RS)-1-(2-methyl-5-nitroimidazole-1yl) propane-2-ol [12]. SEC is sparingly soluble in water [13]. The chemical structure of the SEC is related to tinidazole and metronidazole [14]. It is mainly indicated in giardiasis, amoebiasis, trichomoniasis, and bacterial vaginosis [15]. Secnidazole is a broad-spectrum antibiotic and effective against numerous protozoa, anaerobic Gram-positive and Gram-negative bacteria [16]. Several workers have been used UV-visible spectrophotometer to estimate the quantitative and qualitative analysis of SEC [17-20]. UV-visible spectrometry has been widely utilizing for the determination of riboflavin, cyanocobalamin with the rapid result, high selectivity, accuracy, precision, and sensitivity analysis [21-23].

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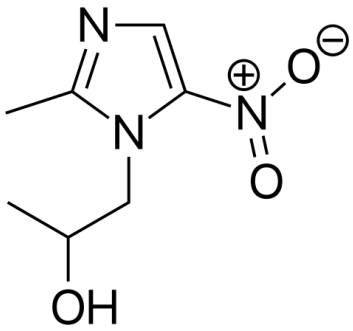

Figure 1. Chemical Structure of Secnidazole

The main objective of the present investigation is to formulate stable SEC gel. The accelerated stability of SEC gel and photolytic studies of SEC in aqueous solution and gel preparations were also carried out. Moreover, the effect of humectants like glycerin (GL) and propylene glycol (PG) on the stability of SEC in the gel was also studied. The work also included the rate constant of photolysis (k_{obs}) of pure SEC solution and gel preparations to find the shelf-life and stabilization ratio.

Materials and Methods

Materials

Secnidazole (98%) was obtained as a gift sample from Nabi-Qasim Industries Private Limited, Karachi, Pakistan with assigned purity. Hydroxypropyl methylcellulose (HPMC, K4M) as a gelling agent, glycerin (GL) (85%), propylene glycol (PG) (≥ 99%), citric acid (monohydrate) (CA), sodium citrate dehydrates, methylparaben (MP), and propylparaben (PP) were purchased from Merck & Co. Whitehouse Station, NJ, USA. Fresh boiled distilled water was applied for the preparation of buffers, SEC solutions, and formulations of SEC gels.

Preparation of SEC Solution and Gels

The formulations of SEC (1% *w/w*) gel were prepared by using different concentrations (2.5-7.5% *w/w*) of HPMC. It was soaked in freshly prepared distilled water at a temperature of 80 °C then allowed to hydrate and swell overnight. PG and GL were added as humectants in the gel preparations. SEC was separately mixed in a mixture of ethanol and distilled water and added to gel preparations. MP and PP were dissolved in hot water and mixed in gel preparations. The solvent blend was transformed into a gel and agitated slowly. Finally, the gels' pH was regulated with citric acid buffer at pH 5.0. The formulation of SEC gels in this study is given in **Table 1.** SEC is sparingly soluble in water. The controlled SEC solution was prepared in a mixture of ethanol and water.

Table 1. Formulation of SEC Gel

Gel Sample	SEC (g)	HPMC (g)	GL (ml)	PG (ml)	MP (mg)	PP (mg)	CA (mg)	SC (mg)	WATER (q.s. to produce 100 g)
G1	1	2.5	7.5	0	0.2	0.04	0.6	0.3	100
G2	1	5.0	5.0	0	0.2	0.04	0.6	0.3	100
G3	1	7.5	2.5	0	0.2	0.04	0.6	0.3	100
G4	1	2.5	2.5	0	0.2	0.04	0.6	0.3	100
G5	1	7.5	7.5	0	0.2	0.04	0.6	0.30	100
G6	1	2.5	0	7.5	0.2	0.04	0.6	0.3	100
G7	1	5.0	0	5.0	0.2	0.04	0.6	0.3	100
G8	1	7.5	0	2.5	0.2	0.04	0.6	0.3	100
G9	1	2.5	0	2.5	0.2	0.04	0.6	0.3	100
G10	1	7.5	0	7.5	0.2	0.04	0.6	0.3	100

pH Measurements

The pH measurements of gel were carried out by Elmetron LCD pH meter (Model-CP 501 sensitivity ±0.01 pH unit, Poland). The electrode was calibrated by using phthalate (pH 4.008) and phosphate (pH 6.865) buffer solutions.

Rheological Properties of SEC Gels

The use of different concentrations of gelling agent HPMC was used to determine the rheological properties like swelling index, viscosity, and spreadability of SEC gel.

Swelling Index

The cross-linked polymer (HPMC) was dispersed in the solvent. The swelling of the polymer defines the change of dimension of a polymer. The swelling value can be calculated by using the following formula at different time intervals.

$$\text{Swelling (\%)} = (Ws - W_d)/Wd \times 100 \quad (1)$$

Where W_d is the Weight of dry polymer and Ws is the weight of the swollen polymer

Viscosity Measurements

The viscosity of the formulated gel was determined by using a rotational viscometer (Brookfield Engineering Laboratories Inc., (Model LVDV–E., USA). A 250 ml of SEC gel was taken into a beaker and pivot dipped into the gel. The viscosity was measured at different angular velocity (30 rpm) by using a spindle No. 5 for 1min, viscosity was recorded at 25 °C. The evaluation was repeated thrice to report for the experimental variability and the mean viscosity was noticed [24].

Light Intensity Measurements

Potassium ferrioxalate actinometry was used to investigate the intensity of the irradiation source and a value of 1.20 ±0.11 × 10^{17} quanta s^{-1} was obtained previously by Arsalan *et al*. [22].

Spectral Measurements

A Shimadzu UV-1601 recording spectrophotometer using quartz cells of 10-mm path length was used for all the absorbance and spectral measurements of control solutions and formulations of SEC gel.

Thin-Layer Chromatography

The photolyzed SEC was extracted with potassium hydroxide (0.1 M) with methanol and subjected to TLC using precoated silica gel 60 F 254 as the stationary phase (E. Merck). The solvent system consists of potassium hydroxide and methanol solution (10:90 *v/v*). This system was found to give a compact spot for degraded and stable SEC. The spots were determined under UV light (209 nm) [25].

Photolysis of SEC

A 1 g of SEC gel was speared uniformly on five glass plates (5×15 cm). The plates were placed in a dark chamber at a persistent humidity and temperature (25±1 °C/ 60% RH) by a Philips HPLN 125 W high-pressure mercury vapor fluorescent lamp, fixed vertically at a distance of 30 cm from the center of the plates. The gels were detached after 30 min exposure to light and were subjected to spectrometric assay.

Accelerated Stability Studies

The SEC gel was packed in aluminum tubes and subjected to stability studies at 40 ± 2 °C / 75% ±5% RH for 6 months. The samples were withdrawn at the time interval of one month and evaluated for rheological properties, pH, physical appearance, and drug content analysis.

Validation of the Assay Method

The assay of SEC was determined by a validated method of UV-visible spectrometric method [17]. The spectrometric method for the assay of SEC was validated based on the guidelines of ICH [26]. Diverse parameters of validation for SEC were investigated which are explained as follows.

Linearity and Range

The linearity was determined by preparing calibration curves of absorbance versus the concentration of SEC of the test solutions in the concentration range of 5-35µg/ml for each preparation. The linearity was statistically defined by regression analysis of five concentrations used in triplicate. The linearity range was selected based on absorbance values in the region of around 0.24-1.75. A standard curve of absorbance versus concentration in the range 5-35µg/ml resulted in the linear least-squares regression equation (r^2 = 0.999) **(Figure 2)**. This range of absorbance is known to offer values with the highest accuracy [27]. The molar absorptivity (A; 1%, 1 cm) values were also determined from the calibration curve.

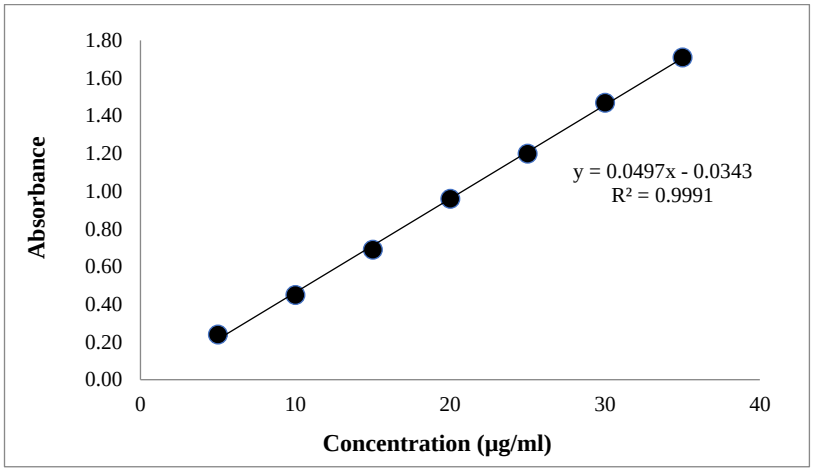

Figure 2. A plot of Absorbance versus Concentration of SEC (µg)

Accuracy

The accuracy of the suggested method was determined by adding specific concentrations of the drug in the solutions, followed by their analysis by the UV-visible spectrometric method. Three different concentrations in triplicate from the studied range were selected and analyzed for the recovery.

Precision

The precision of the developed method was calculated by conducting nine determinations at various concentrations covering the specified range. The precision was determined by calculating the relative standard deviation (% RSD) of the mean recoveries.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

LOD and LOQ of the developed method were calculated from the standard deviation of the *y*-intercept and slope of the calibration curve using the following formulae:

$$LOD = 3.3 \times \frac{\sigma}{S} \quad (2)$$

$$\mathrm{LOQ} = 10 \times \frac{\Sigma}{S} \quad (3)$$

where σ is the standard deviation of the intercept and *S* is the slope of the calibration curve.

Robustness

The robustness of the method was determined by studying small changes in the assay wavelength (±2 nm). This parameter was studied thrice in the similar range used for the determination of SEC (i.e., 5-35µg/ml).

Results and Discussion

Formulation of SEC Gel

The effect of concentration of gelling agent (HPMC) and humectants (GL and PG) in the formulations of SEC gel has been studied. The change in the concentration of HPMC may affect the swelling index of gel in the formulation **(Table 2)**. It has been found that humectants may affect the rheological properties of SEC gel formulations and play an important role in the stability of SEC gel formulations. There is a change in viscosity due to differences in the concentration of HPMC, GL, and PG was observed in different formulations (G1-G10) **(Table 3)**. The viscosity of the gels may affect the Physico-chemical and rheological properties like transparency, homogeneity, and consistency.

Table 2. Swelling Index of HPMC

HPMC	Time(Hour)	Swelling Index (%)
2.5%	At 1hour	77
	At 4hour	83
	At 8 hour	100
5.0%	At 1hour	85
	At 4hour	94
	At 8 hour	100

	At 1hour	90
7.5%	At 4hour	96
	At 8 hour	100

Table 3. Effect of HPMC, GL, and PG on the Viscosity of SEC Gel Preparations

Gel Sample	SEC (g)	HPMC (g)	GL (ml)	PG (ml)	VISCOSITY (centipoise)
G1	1	2.5	7.5	0	3200
G2	1	5.0	5.0	0	4250
G3	1	7.5	2.5	0	5350
G4	1	2.5	2.5	0	3350
G5	1	7.5	7.5	0	5250
G6	1	2.5	0	7.5	3100
G7	1	5.0	0	5.0	4050
G8	1	7.5	0	2.5	5250
G9	1	2.5	0	2.5	3250
G10	1	7.5	0	7.5	5200

Photodegradation of SEC

Light may influence the rate of photolysis of photosensitive drugs. SEC is sensitive to light. The photolysis of SEC was increased in the presence of light due to high energy content in irradiation. The use of different concentrations of HPMC and humectants in the formulation of gel may affect the photolytic degradation of SEC. The pure solution and gel preparations of SEC were photolyzed to determine the first-order rate constant (k_{obs}) and the aqueous solution was treated as a reference standard to determine the shelf-life and stabilization ratio of SEC in gel preparations **(Table 4)**.

Table 4. First–order Constants (k_{obs}) for the Photolysis of SEC in Aqueous and Gel Preparations with Shelf-lives (t_{90}), Stabilization Ratio

Samples	$k_{obs} \times 10^{-2} \pm$ SD min^{-1}	t_{90} of Photolyzed SEC (min)	Stabilization Ratio
Pure Solution	11.81	8.891	-
G1	5.51	19.056	2.143
G2	4.60	22.826	2.567
G3	4.11	25.547	2.873
G4	5.54	18.953	2.132
G5	3.92	26.786	3.013
G6	5.58	18.817	2.116
G7	4.89	21.472	2.415
G8	4.54	23.128	2.601
G9	6.03	17.413	1.958
G10	4.20	25.000	2.812

Thin Layer Chromatography Outcomes

The purity and identification SEC were evaluated by TLC. The TLC of photolyzed SEC in gels and emulgels have shown reduction in the size of the spot as compared to pure SEC by using a solvent system consisting of potassium hydroxide and methanol solution (10:90 *v/v*) under UV light at 209 nm.

Assay for SEC

The assay of pure and photolyzed SEC in aqueous and gel formulations has been carried out in an alkaline medium (pH 9.0) by using a UV-visible spectrophotometer. Shovkova *et al*. [17] have used this method for the assay of SEC. The quantity of the drug was calculated from the standard calibration curve. The equivalent amount of SEC (~10 mg) from the solution was diluted in 50 ml water to make it a 200 µg/ml SEC concentration stock solution. The stock solution was converted into 5-35 µg/ml SEC concentration for analysis. Similarly, SEC gel formulations (1% *w/w*) were diluted in 100 ml water to get 10 mg of SEC concentration in a diluted solution. This dilution was further diluted to produce 20 µg/ml SEC concentrations for analysis. The photodegraded product of SEC was observed at 209 nm.

The samples were scanned in UV-visible spectrophotometer from a range of 200-600 nm against potassium hydroxide (0.1 M) as a blank. The λ_{max} of every sample was measured at 318 nm. It was estimated frequently by analyzing the standard stock of SEC which gives repeated results on (intra-day) and intermediate precision (inter-day).

Spectral Evaluation and Spectrometric Assay

A pure aqueous solution of SEC has shown its peak at 277, 311, and 320 nm in acidic (5.0), neutral (7.0), and alkaline (9.0) pH. The formulations of SEC gel (pH 5.0) were photolyzed for 150 min and measured the reading after 30 min intervals. The gradual loss in SEC peak after exposure of light was observed. Moreover, the peak of the degraded product of SEC [(2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1,5-dione)] was not observed at acidic pH (5.0) and neutral pH (7.0). The peak of degradation product of SEC in spectra was observed in an alkaline medium. There was a steady loss in the peak of SEC in the gel from 318 nm to 315 nm with an increase in a peak at 209 nm due to the formation of a photoproduct of SEC [(2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1,5-dione)] in alkaline medium. It has been observed that the prolonged exposure of SEC has diminished the peak of degraded product at 209 nm.

Accelerated Stability Studies

The accelerated stability studies of SEC gel formulations were conducted at 40 ± 2°C at 75 ± 5% RH for six months. The formulations of SEC gels were observed to be a smooth homogeneous transparent viscous preparation. Thus, the formulations were found to be stable under stressed conditions **(Table 5)**. There was no evidence of syneresis in the gels which was a common drawback of gels.

Table 5. Accelerated Stability Study of GL (G1-G5) and PG (G6-G10) Preparations

Months	Drug				Content (%)					
	G1	**G2**	**G3**	**G4**	**G5**	**G6**	**G7**	**G8**	**G9**	**G10**
0	100	100	100	100	100	100	100	100	100	100
1	98.44	98.34	98.98	98.23	98.76	98.27	98.7	98.37	98.35	98.67
2	96.98	96.67	97.42	96.79	97.54	97.34	97.5	97.01	96.23	96.66
3	95.73	95.01	96.02	95.69	96.35	95.05	95.5	95.89	94.76	95.23
4	94.77	94.56	95.22	94.7	95.33	93.78	93.9	94.69	93.21	93.77
5	93.99	93.45	94.42	93.81	94.4	92.74	92.5	93.57	92.01	92.34
6	91.89	92.1	93.45	92.84	93.71	91.82	91.3	92.48	90.43	91.02

Formulation of SEC Gels

The SEC gel preparations were transparent in appearance. All formulations of SEC gels were prepared for healthy skin pH (5.0). The SEC gels were uniformly mixed and consistent in appearance, with no segregation or any other signs of instability. The grittiness was not visually observed and found complete homogenization after applying them on the front of hands. The increase in the concentration of humectants (GL and PG) has increased the spreadability of the formulations with the least concentration of HPMC. PG has shown better spreadability as compared to GL. Rao *et al*. [28] has also found more spreadability in less viscous emulgels.

Accelerated Stability of SEC Gel

SEC is stable against hydrolytic degradation [14]. It has been observed that GL containing gel preparation possessed more stability as compared to PG. GL possessed more viscosity compared to PG [29]. GL is stable to atmospheric oxidation but readily oxidized in the presence of oxidants. In the present study, the formulation of SEC gel preparations is considered critically.

The stability profile concerning time has been noted in **Table 5**. The degradation of SEC gels in accelerated stability studies is slow and negligible which indicated good stability. The chemical structure of the SEC is similar to metronidazole. The formulations of SEC gel were adjusted at pH 5.0 because of equivalence to the pH of healthy skin. Metronidazole possessed fast degradation at 2.0 pH followed by 6.0 pH, whereas, greater stabilization at pH 4.0 [30].

The degradation of drugs usually followed the first-order kinetics. Wu and Fassihi have found that metronidazole possessed proper stability in the solid-state under the accelerated conditions (40 ºC, 75% RH) for 3 months. The degradation of metronidazole has also shown apparent first-order kinetics with a very slow degradation rate constant [31]. The fractions of protonated species of metronidazole were less noted at pH 5.0 this is maximum stabilized at pH 4.0-6.0 [32]. The accelerated stability of metronidazole is ~ 6 fold in propylene as compared to the aqueous solution [33].

The rate of degradation of SEC was found to have a linear relation with the concentration of HPMC. The increase in the concentration of HPMC has been increasing the stability of the SEC in gel preparation due to an increase in viscosity. SEC is stable to dry heat. The degradation of SEC by oxidative stress is significantly observed. The use of citric acid in the preparation is not only as a buffer but it is also used as an antioxidant and also possessed anti-inflammatory action [34]. Thus, the degradation of SEC gel was found negligible. It has been observed that SEC gel preparation in PG is a more stable preparation as compared to GL.

Application of the Assay

The photochemical method has been applied to the assay of SEC in fresh and accelerated stressed gel preparations. The accuracy and precision of the method have been specified, and its sensitivity has been validated. The method is stability-

indicating for the assay of SEC in gel preparations based on the amount of photodegraded formed under accelerated stressed conditions and its quantitative relationship with the ratio of SEC. A similar photochemical method for the assay of riboflavin and thiamine based on the formation of its photoproduct has been reported [27, 35]. The formation of an isosbestic point at 295 and 237 nm has proved the formation of a single photodegraded product (2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1,5-dione) has shown peak at 209 nm. The method is stability-indicating for the assay of SEC in gel preparations based on the amount of photodegraded formed under accelerated stressed conditions and its quantitative association with the ratio of SEC.

Photolysis of SEC

The photolysis of SEC in aqueous solution may yield a photodegraded product (2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1,5-dione) at 209 nm. The formation of 2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1, 5-dione photodegraded product was mainly due to photo oxidation of SEC. It has been supposed that endoperoxide may lead to the transformation to the dioxetane intermediate which then forms the end product nitro imidazole drugs may undergo photo oxidation and results in the decrease in intensity of absorption [36]. The rate of photolysis of SEC least found in G5 formulation is mainly due to the increase in viscosity. The increase in viscosity of formulations has played a major role in the reduction of the rate of photolysis of SEC in gel formulations. Thus, the formulations of SEC gel containing GL as humectant possessed more photo stability compared to gel formulation containing PG and aqueous solution of pure SEC. The viscosity of GL containing formulations may decrease the penetration of oxygen. The effect of the different concentrations of HPMC in gel formulations has also played a major role in the photo stabilization of SEC in gel preparations.

Thin Layer Chromatography of SEC

The formation of a photodegraded product by the UV photolysis of SEC in various formulations of gels and emulgels has been studied by TLC. The constant loss of SEC in aqueous solution and gel and emulgel formulation has been shown by the loss in absorption in the UV region. All the formulations of gels and emulgels showed the loss of SEC on detection by TLC. The rate of photo degradation of SEC was last observed in the formulation (G5). The lesser degradation of SEC in gels was proved by the greater intensity of SEC spot compared to the control solution. Similarly, the photo degradation of riboflavin was observed by Ahmad *et al*. [23]. Mainly, the intensity of SEC spot of gel and emulgel was reduced with the increase in exposure of irradiation but due to difference in formulation ingredients, the rate constant of photolysis may vary which may affect the spot of SEC in different formulations of gels. The formation of (2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1,5-dione) by photo oxidation of SEC solutions has previously been reported by Larina and Lopyrev [36].

Absorption Characteristics of Photolyzed SEC

The spectra of an aqueous solution of pure SEC has been shown a peak at 277 nm in acidic pH (5.0). There is a gradual loss in the intensity of absorption of photolyzed SEC solution with an interval of 30 min. The peak of end photodegraded product of SEC, [2, 4-(N-2- hydroxypropyl) diaza-3-methyl-1-nitro-1,5-dione] was not shown in acidic medium. Similarly, in a neutral medium (pH, 7.0) the peak of photodegraded was also not observed, whereas, in an alkaline medium a bathochromic shift of pure SEC solution was observed at 320 nm due to an increase in pH. The absorption peak has been shifted due to the change in pH [37]. The absorption spectra of photolyzed gel formulations of SEC at alkaline pH (9.0) indicated the presence of isosbestic point around 295 nm indicating the transformation of SEC into a photodegraded product [25]. The peak of the photo degradation product of SEC in the gel has not been found after a longer period of light exposure [38]. It has been observed that after long irradiation the peak of the photodegraded product was diminished. A similar case was reported by Larina and Lopyrev [36].

Kinetics of Photo degradation of SEC

The photo degradation assay data of SEC in gel formulations was found to follow apparent first-order kinetics like metronidazole [39]. The apparent first-order rate constant (k_{obs}) were obtained by the plots of log concentration against time was reported in **Table 4**. It appears that the formulation characteristics of SEC gels greatly affect the rate of reaction, and hence these factors are discussed in the following sections.

Effect on the Viscosity of Gel

The consistency of gel formulation depends on the viscosity. There is an increase in viscosity of SEC gel formulations by the increase in the concentration of HPMC (K4M). The increase in shearing force decreases the viscosity of gels showed with the non-Newtonian flow; mainly this has been occurred due to its low flow resistance when applied at high shear conditions. The decrease in viscosity is due to pseudo plastic behavior as observed in the SEC gel formulations. It has been observed that the characteristic of high spread ability is mainly due to the decrease in viscosity. The increase in viscosity of gel has decreased the photo degradation of the SEC in the gel.

Effect of Humectant on SEC Gel

Humectants are used to keep the preparation moist and miscible with water. They improve the spread ability. The viscosity of GL and PG is varying ~935 and ~41 mPa/s, respectively [29]. A linear relationship of photo degradation versus the reciprocal of viscosity indicates the rate of photo degradation depending on the viscosity of the medium. It mainly affects the

stability of oxidizable drug substances. SEC is metabolized by oxidation. The plot indicates the highest rate of photolysis was observed in G9 due to the lowest concentration of PG and HPMC and highest in G5 due to the highest concentration of GL and HPMC. The photo degradation of cyanocobalamin in an aqueous solution was suppressed by the addition of GL.
The lesser penetration of oxygen in the medium in more viscous preparation has reduced the chances of photo oxidation of SEC. Cairns has found that riboflavin reacted with glycerin which acts as an electron donor but with the increase in viscosity by the use of 100% GL the rate of photolysis of riboflavin was reduced due to an increase in viscosity [27]. The viscosity of 100% glycerin was also affected by the decrease in quantum yield. Thus, photo stabilization is achieved by the increase in viscosity.

Conclusion

The formulation of SEC gel preparation is the most stable at 7.5% HPMC containing GL and PG as humectants. The Physico-chemical and rheological properties of SEC gel-like transparency, homogeneity, consistency, spreadability, and film-forming abilities are negligibly changed. The increase in the viscosity of gel decreases the penetration of oxygen and aids in the reduction of oxidative stress in accelerated stability studies. The gel preparations are also stable against the light. The photo degradation of the SEC is minimized by the use of citric acid buffer and the viscosity of humectants should be considered in the gel formulations to achieve photo stabilization.

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