Table 7. Solutions Obtained from Numerical Optimization.

Solution No.	Liquid Lipid	Homogenization Speed	Desirability
1	3.5	7000	1.000
2	3.5	5000	1.000
3	3.5	3000	1.000
4	2.3	3400	1.000
5	5	3000	1.000
6	2.3	5400	1.000
7	2.3	6600	1.000
8	5	7000	1.000
9	5	5000	1.000
10	4.9958	3366	1.000
11	4.1621	6548.4	1.000
12	3.1709	6530.8	1.000
13	4.6154	5360.8	1.000
14	3.8807	5766.8	1.000
15	2.6552	3950.8	1.000
16	3.7718	3675.2	1.000
17	3.2552	5136.4	1.000
18	3.92	4298.8	1.000
19	4.0421	5518.4	1.000
20	3.47	3060.8	1.000
21	4.8083	5944.8	1.000
22	4.9766	5902.4	1.000
23	2.3321	4724	1000
24	4.5398	5233.6	1.000
25	4.3541	6228.4	1.000
26	4.3313	6342.4	1.000
27	2.0468	3498.4	1.000
28	2.5997	3856	1.000
29	3.8339	3488	1.000
30	4.7573	5917.6	1.000
31	3.8864	5560	1.000
32	4.6277	5663.2	1.000
33	3.1544	5865.6	1.000
34	3.4685	5661.6	1.000
35	4.271	6238.4	1.000
36	3.8429	6912.8	1.000
37	2.1683	4212.8	1.000
38	3.9455	4045.2	1.000
39	2.7617	6806.8	1.000

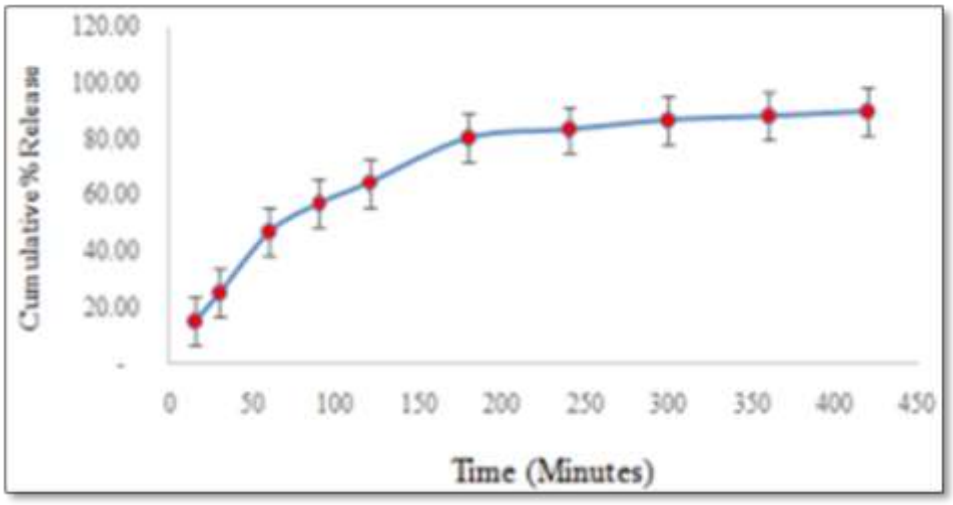

Figure 8. Cumulative % Release of Ofloxacin from Optimized Formulation (Nlc_1) in Phosphate Buffer Ph7.4 *Ex-vivo* Permeation Study using Goat Skin.

An *ex-vivo* experiment was carried out to verify the correlations between the *in-vitro* drug diffusion investigation and the dialysis membrane experiment. The outcomes were good enough to move forward. It has been decided to use healthy adult goat ocular skin for this experiment (drug permeation kinetics). The order revealed by skin permeability is as follows: mouse > rat > guinea pig > rabbit > monkey > dog > goat > ship > pig > human [32]. It has been discovered that the optimized product penetrates the goat ocular surface with Ofloxacin at a rate of around 71.33% in 7 h.

Zero-order kinetics could be used to describe drug penetration. Using P = K, the permeability coefficient was computed. Vr/S, where Vr is the receiver chamber's volume, S is the goat ocular skin's effective surface area, K is the zero-order constant, and P is the permeability coefficient of 26. The measured speed was 1.141 cm/min [33] (**Figure 9**).

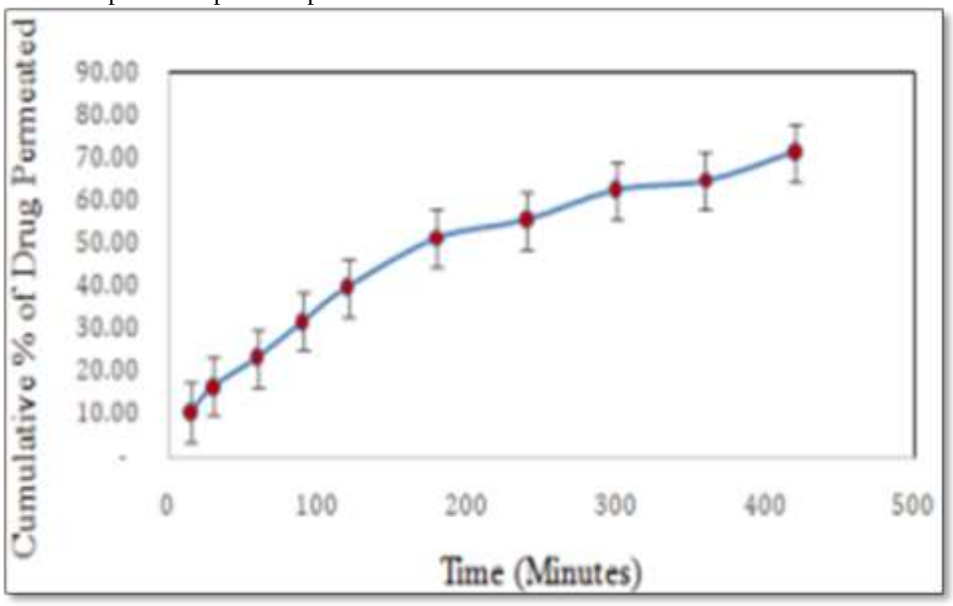

Figure 9. Cumulative % of Ofloxacin Permeated.

DISCUSSION

As was previously mentioned, Ofloxacin-loaded NLC was used in this investigation. The purpose of the study was to assess the Ofloxacin-loaded nanogel's suitability for optical delivery. First, an FTIR study was used to assess the drug's compatibility with the excipients. It is possible to proceed with nanogel formulations using this combination, according

to the interpretation of the FTIR spectra. Design-Expert software (Version 7.1.5) was used to develop the formulations using a face-centered Central Composite Design in order to optimize the formulation based on particle size, spreadability coefficient, and percentage entrapment efficiency. 13 formulations with 5 repetitions were offered by the software to check and analyzes errors. The Ofloxacin-loaded NLC formulations' percentage entrapment efficiency was determined to be between 48.7% and 93.05%, and their particle size measurements indicated that they ranged from 78.79 nm to 648.4 nm. Ofloxacin-loaded nanogel formulations were shown to have a spreadability between 0.259 and 0.359 gm. cm/sec. The findings were analyzed using the ANOVA. To explain the effect of Independent Variables (Factor) on the response parameter particle size, spreadability coefficient, and percentage entrapment efficiency, polynomial equations and the software's produced 3D response surface graphs were utilized. Based on the response parameter values, the software generated 39 optimal formulation predictions. Among the formulations, one with a small particle size was selected to conduct the extra investigation. Verification of the particle size distribution and surface morphology was achieved by examining the SEM photograph of the formulation. The particle size of the optimized formulation was found to be between 67.69 and 170.9 nm by performing an SEM inspection.

The *ex-vivo* penetration of the optimized formulation through goat optical skin and the *in-vitro* drug diffusion utilizing a dialysis membrane were both examined using a Franz diffusion cell. The 7 h were dedicated to the in vitro drug diffusion investigation. After 5 h, it was noted that the drug diffusion from the optimized formulation grew steadily and then stabilized. After 7 h, the Ofloxacin diffusion rate was 897.79 percent.

To verify the correlations between the *in-vitro* drug diffusion investigation with a dialysis membrane and the *ex-vivo* experiment, the former was carried out first. The findings were sufficient to move forward. The optimized solution has been discovered to have about 71.33% penetration rate of Ofloxacin through goat ocular skin in just 7 h. Zero-order kinetics could be used to describe drug penetration. Using P = K, the permeability coefficient was computed. The formula is Vr/S, where S is the goat ocular skin's effective surface area, Vr is the receiver chamber's volume, K is the zero-order constant, and P is the permeability coefficient. The measured speed was 1.141 cm/min. As a result, we may conclude from the results of this investigation that the NLC formulations effectively distribute Ofloxacin through the ocular membrane. These investigations will help to improve the formulation in the future for usage in ocular medication delivery scenarios.

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