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Improvement Of Quercetin-Loaded Eudrgit L- 100 Nanoparticles Using Factorial Desgin Methadology

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ABSTRACT

Background: Quercetin is a flavonoid with strong antioxidant properties with a wide range of pharmacological actions. The aim of this study was to see how formulation parameters affected the physicochemical characteristics of quercetin-loaded polymeric nanoparticles so that the formulation might be improved.

Materials and procedures: Nanoprecipitation was used to create the nanoparticles. This study used a Box-Behnken design with three levels and three factors using Eudragit L-100, Pluronic F-68 concentration, and volume of organic solvent as independent variables. Particle size, polydispersity index, and zeta potential as response.

Results: The amount of polymer is the most important factor influencing quercetin-nanoparticle characteristics. Increasing amount of Eudragit L-100 led to an increase in particle size and,. Polydispersity index .As opposed to that, it exhibited a slightly positive influence on zeta potential.

The pluronic concentration had positive effect on particle size and polydispersity index. However, pluronic concentration had an important negative effect on the zeta potential. .The volume of organic solvent had an negative effect on the particle size and zeta potential but positive effect on PDI. Based on An improved formulation was created based on the results, and the experimental values were close to those expected.

Conclusions: Overall, the amount of polymer EDRAGIT L-100 used had the greatest impact on particle size, while the pluronic F-68 concentration had the greatest impact on PDI and zeta potential

Keywords: *nanoparticle, quercetin, experimental design, Box-Behnken, optimization*

INTRODUCTION

Nanoparticles have attracted a lot of attention in recent years. Because they have the potential to be used as drug delivery systems. Colloidal systems called polymeric nanoparticles range in size from 10 to 1000 nanometers. They consist of biodegradable polymers that have the active component chemically or adsorbably bound to the matrix of the polymer. [1]. High stability, the ability to Both hydrophilic and hydrophobic compounds, entrapment of the chemical from enzymatic degradation, delivery via various channels, decrease of administration frequency, daily dosages, and adverse effects are all factors to consider. all advantages of nanoparticulate carriers [2-4].In addition to ensuring cell targeting, nanoparticles can extend the duration of poorly absorbed drugs in the body, permit controlled release, and increase their bioavailability [4-5]. Eudragit polymers are adaptable polyacrylate polymers with varied degrees of solubility, making them appropriate for formulations with a long release time [44]. It was initially offered in the 1950s by Evonik Industries [45], and it was manufactured in Darmstadt, Weiterstadt. Rohm Gmbh and Co. KG, Darmstadt, Germany, is the owner of this trademark. It was made by polymerizing acrylic and methacrylic acids or their esters, whose physicochemical characteristics are controlled by the R- functional group. USPNF, BP, Ph Eur, and the Handbook of Pharmaceutical Excipients [45] have all included Eudragit as a new excipient The use of coating polymers such as Eudragit L-100 is recommended. They allow you to target specific portions of the intestine. These anionic Eudragit grades disintegrate when the PH level rises. In addition, different grades can be combined and matched with one another. The Eudragit L polymers are the most popular coating polymer. They make it possible to target specific parts of the gut. At higher PH levels, these anionic Eudragit grades disintegrate. Furthermore, various grades may be mixed and matched, allowing the dissolution pH to be adjusted and therefore the drug's GI targeting to be achieved [45]. pH-dependent medication release, increased drug efficacy, improved storage stability, colon targeting, and protection of actives sensitive to stomach fluid are just a few of the benefits

Eudragit offers for enteric coatings. Eudragit L-100 polymers are methacrylic acid and ethyl acrylates copolymers. These are anionic, white, free- flowing powders having a molar mass of around 125,000 g/mol. Effective and stable enteric coatings with rapid dissolution in the upper bowel, granulation of drug substances in powder form for controlled release, site-specific drug delivery in the intestine by combining Eudragit S grades.

in contrast to traditional medication delivery methods The stabilizing agents are among the components utilized in the creation of nanoparticles. They function by stabilizing the colloidal system and reducing the interfacial tension between hydrophilic and hydrophobic surfaces.. Non-ionic chemicals like pluronic (F-68) or other forms of PVP are favored to others, particularly when it comes to adding water-insoluble ingredients [3] converting substances to nanoparticle.

Quercetin (3,3',4',5,7-pentahydroxyflavone, QU is a flavonoid that may be found in a variety of fruits, vegetables, -based foods [6]. The biological properties of QU include immunomodulatory, antiviral, anti-proliferative, anti-allergic, anti-inflammatory, antioxidant, and anti-carcinogenic effects [7, 8, 9, 10, 11]. Because of the great quantity and location of hydroxyl groups, as well as conjugated orbitals, QU is regarded one of the finest antioxidant flavonoid [12]. However, due to its low water solubility, fast metabolic rate, , and instability in physiological media, its clinical utility is restricted. Low bioavailability is the outcome of all of these factors [9,13,14].

QU entrapment in a nanoscale delivery device, which might improve the drug's pharmacokinetics, pharmacological properties, and solubility [15,16], could solve these concerns Nanoprecipitation, emulsification, solvent diffusion, solvent evaporation, and salting out are some of the most common processes for creating nanoparticles [4]. The solubility of the active ingredient determines which approach is used [2]. The nanoprecipitation approach is most commonly used for lipophilic compounds with

low water solubility but high solubility in organic solvents like ethanol or acetone [17]. This approach entails mixing a polymer and drug organic solution in an aqueous media, then evaporating the organic solvent [18]. It's a straightforward, rapid, and repeatable process [19] that yields nanoparticles with a diameter of roughly 200 nm [20].

The physicochemical characteristics of polymeric nanoparticles are influenced by the materials employed, including the polymer, stabilizing agent, and active ingredient, as well as other process factors [44]. In order to achieve therapeutic effectiveness, and the development of drug delivery systems is to contain enough medicine to create an ideal concentration at the site of action. so early on in the development process, characteristics affecting both the nano-carrier and the medicine must be examined [21] .Traditional trials are time-consuming and require more labor and materials when generating a complicated composition [22]. By doing a limited number of tests, experimental design technique allows researchers to explore several factors at the same time, their relationships, and their impact on various experimental responses [23]. It may also calculate the optimal level of variables necessary for a specific response using mathematical models [22]. This approach may be utilized to improve nanoparticle preparation conditions successfully [24] The effects of three formulation parameters on the properties of QU nanoparticles were investigated in this work .To provide an effective technique of optimizing the preparation conditions of the polymeric nanoparticles, an experimental design was adopted. This method entailed analyzing response surfaces in order to determine the link between the components of the experiment and the result, as well as to come up with a suitable formulation. .

TABLE 1: Independent variables and their levels of variation

Levels						
Variables			**Units**	**-1 (Low)**	**0 (Medium)**	**+1 (High)**
Independent variables	**X1**	**Volume of organic phase**	**ml**	**5**	**7.5**	**10**
	X2	**Concentration of surfactant**	**% (m/V)**	**0.5**	**1**	**1.5**
	X3	**Amount of Polymer**	**mg**	**5**	**10**	**15**

MATERIALS AND PROCEDURES

QU-nanoparticle preparation

The solvent displacement approach, commonly known as the nanoprecipitation method, was used to create QU-nanoparticles. Briefly, 5–10 ml of 100% ethanol were used to dissolve the relevant amount of Eudragit L100 (50–150 mg). Drop by drop, the resultant organic solution was added to an aqueous Pluronic (F-68) solution at a particular concentration (0.5–1.5%) while being stirred magnetically at a predetermined rotation speed. To fully eliminate the formulation's organic solvent, the mixture was kept under continuous magnetic stirring for (2 – 4.5) hours under R.T. without heating.

Characterization of QU nanoparticles using physicochemical methods

Particle size and PdI

Using a Zetasizer Nano-ZS90, dynamic light scattering was used to measure the polydispersity and particle size of QU-nanoparticles (Malvern, UK). Then, 50 l of a nanoparticle suspension in double-distilled water were examined. Three measurements were made for each sample. The computed PdI supported the particle distribution.

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Zeta potential

Zetasizer Nano-ZS90 electrophoretic light scattering was used to estimate the surface charge of the QU-nanoparticles (Malvern, UK). Double distilled water was used to dilute the nanoparticle dispersion. Measurements were taken in triplicate.

TABLE 2 : Design matrix

Formulation Code	Experiment NO.	Volume of organic solvent (X1)	Pluronic concentration (X2)	Amount of polymer (X3)
Q1	**1**	**10.00**	**1.00**	**100.00**
Q2	**2**	**7.50**	**1.50**	**100.00**
Q3	**3**	**7.50**	**1.00**	**100.00**
Q4	**4**	**7.50**	**1.50**	**100.00**
Q5	**5**	**7.50**	**1.00**	**150.00**
Q6	**6**	**7.50**	**0.50**	**100.00**
Q7	**7**	**7.50**	**1.00**	**50.00**
Q8	**8**	**5.00**	**0.50**	**100.00**
Q9	**9**	**7.50**	**1.00**	**100.00**
Q10	**10**	**10.00**	**1.50**	**100.00**
Q11	**11**	**7.50**	**1.00**	**100.00**
Q12	**12**	**7.50**	**1.00**	**100.00**
Q13	**13**	**7.50**	**0.50**	**50.00**
Q14	**14**	**7.50**	**1.00**	**150.00**
Q15	**15**	**7.50**	**1.50**	**150.00**
Q16	**16**	**5.00**	**1.00**	**50.00**
Q17	**17**	**5.00**	**1.00**	**150.00**
Q18	**18**	**10.00**	**1.00**	**100.00**
Q19	**19**	**7.50**	**1.00**	**50.00**
Q20	**20**	**7.50**	**0.50**	**100.00**
Q21	**21**	**7.50**	**1.50**	**50.00**
Q22	**22**	**10.00**	**1.00**	**150.00**
Q23	**23**	**5.00**	**1.00**	**100.00**
Q24	**24**	**7.50**	**1.00**	**100.00**
Q25	**25**	**5.00**	**1.50**	**100.00**
Q26	**26**	**7.50**	**0.50**	**150.00**
Q27	**27**	**5.00**	**1.00**	**100.00**
Q28	**28**	**10.00**	**1.00**	**50.00**
Q29	**29**	**10.00**	**0.50**	**100.00**

RESULTS

Preparation and characterization of QU-nanoparticles

The experimental results concerning particle size, PdI, and zeta potential from all experiments are given in Table 3

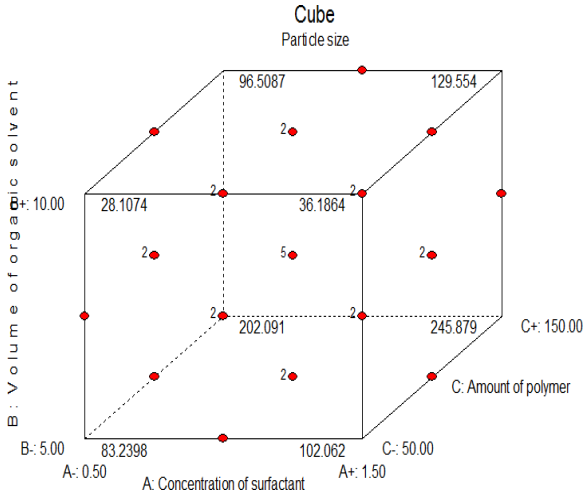
Experimental design analysis. Fitting the model

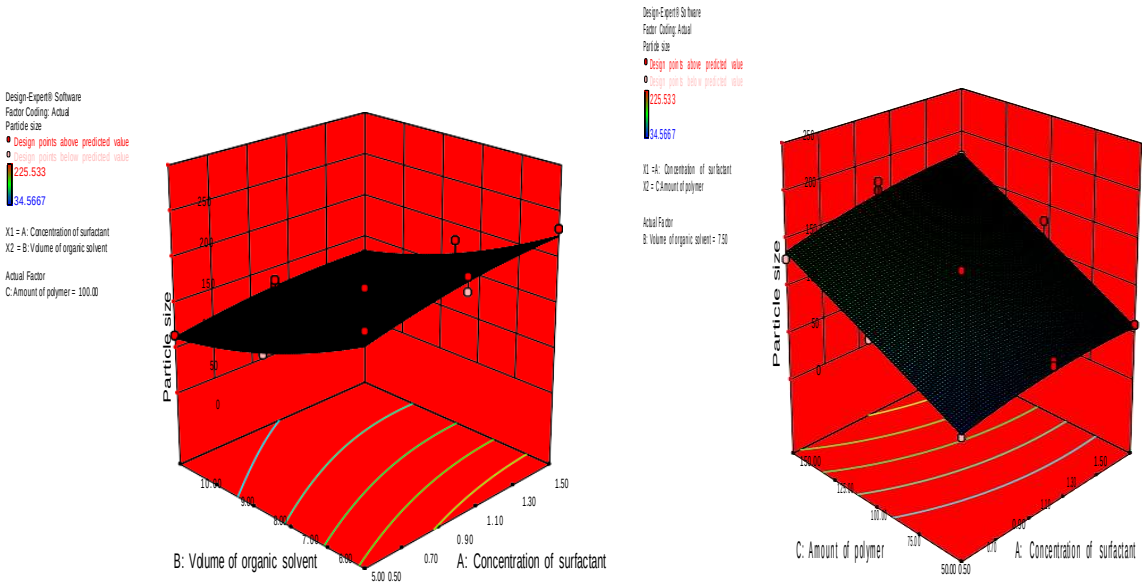
In order to suit the experimental data to the desirable model and to test the validity of the experimental design, Observed values of the quadratic parameter for particle size and PDI and linear parameter for zeta potential were calculated (Table V) and analysis of variance (ANOVA) was performed. The fitted model is taken into account adequate if the model is important ($P < 0.05$) and therefore the lack of fit isn't significant ($P > 0.05$).

Experimental design analysis. Regression coefficients analysis

The regression coefficients and their influence on each of the three responses are presented in cubic graph A,B,C positive value of the parametric

statistic indicates a positive effect on the response, while a negative value suggests an inverse relation between the formulation factor and therefore the response [27, 28]. To illustrate the influence of the formulation factors on the responses, three-dimensional response surface curves were plotted.in cubic graph for every response are shown in Figures (1-3).





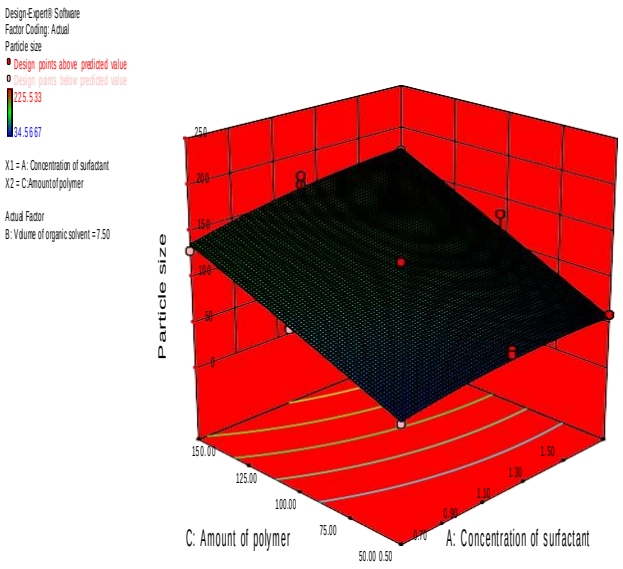
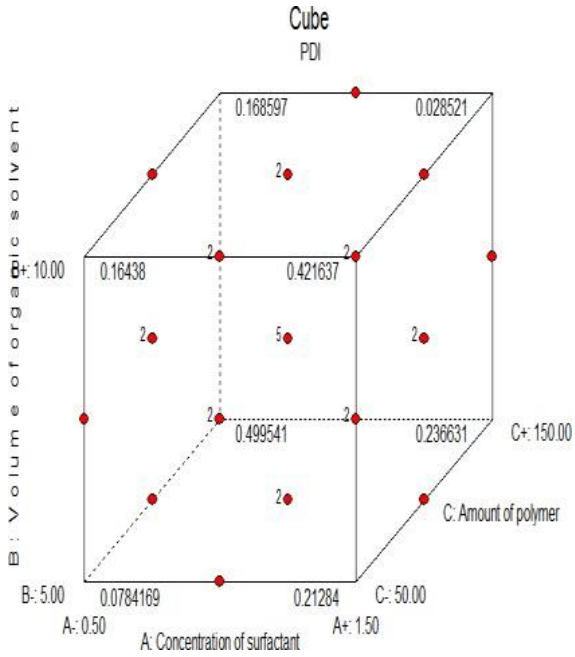


FIGURE 1.(A) Cubic graph response surface Plots in three dimensions illustrating how formulationvariables effect on particle size (Y3):; X1 – Amount of Eudragit L100; X2 – Pluronic (F-68) concentration; X3–volume of organic solvent.



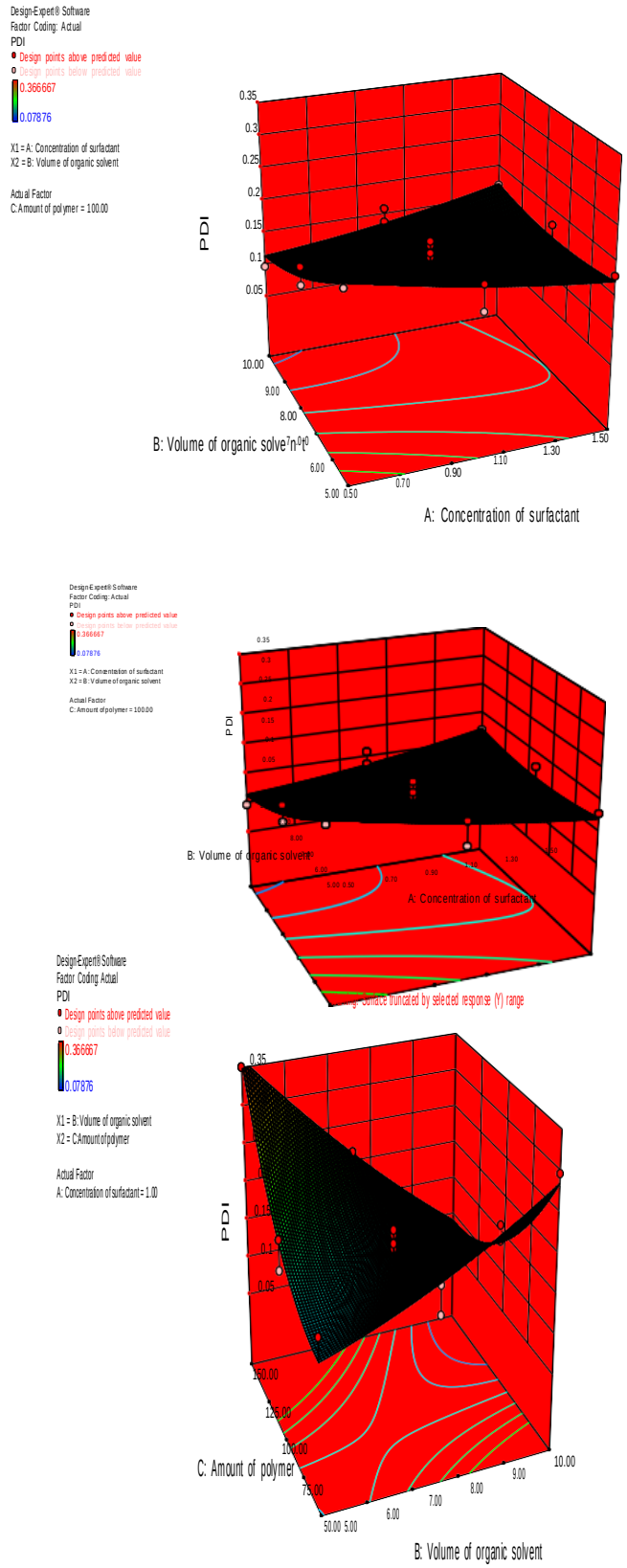


FIGURE 2. (B) Cubic graph response surface and Plots in three dimensions illustrating how formulation variables affect on PDI (Y3):;X1 – Amount of Eudragit L100; X2 – Pluronic (F-68) concentration; X3 – volume of organic solvent

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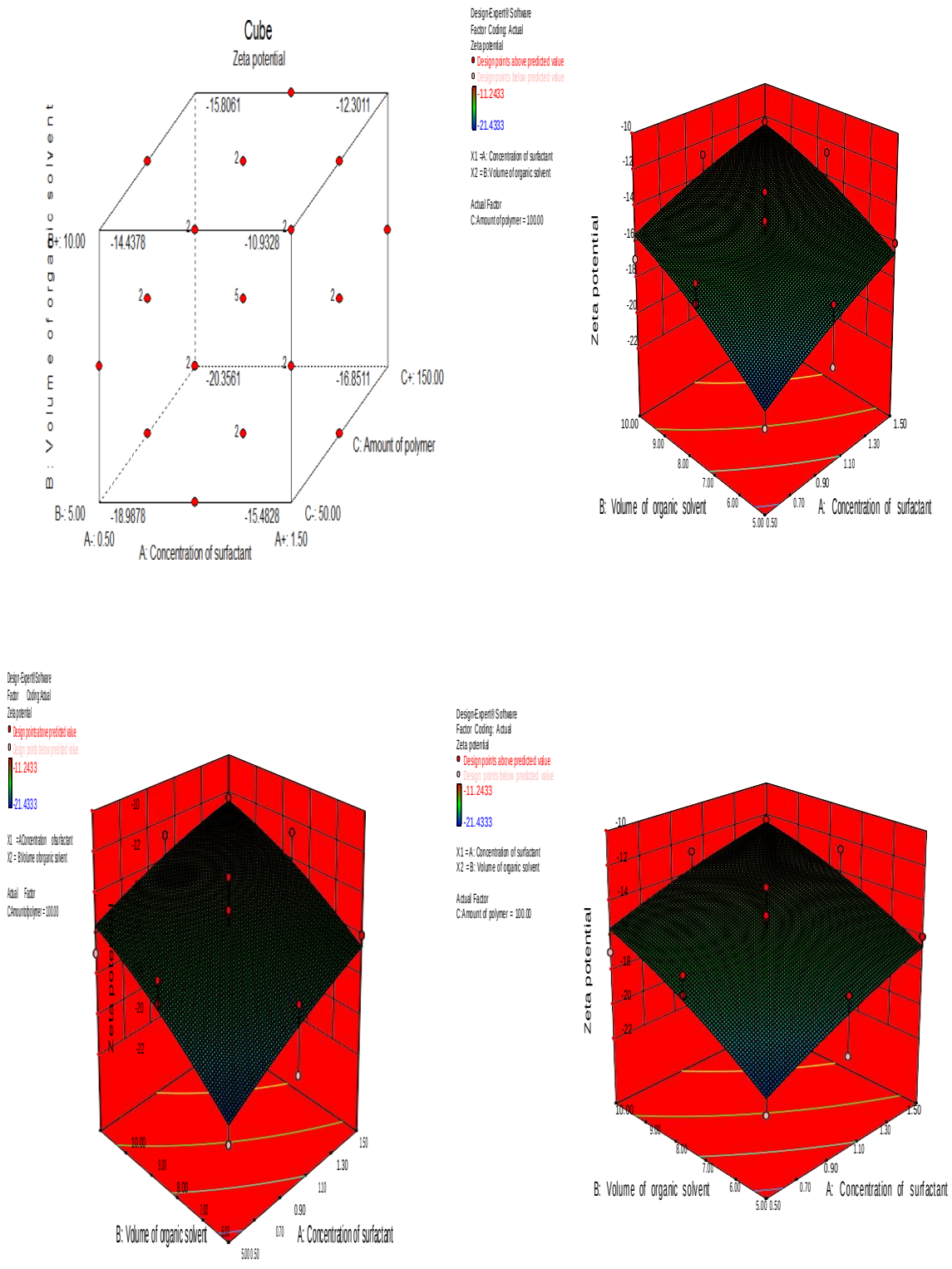

FIGURE 3. (C) Cubic graph response surface and Plots in three dimensions illustrating formulation variables affect zeta potential (Y3):; X1 – Amount of Eudragit L100; X2 – Pluronic (F-68) concentration; X3 – volume of organic solvent

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TABLE 3: Results for particle size (Y1), zeta potential; (Y2), PDI (Y3)

Formulation Code	Run No.	Volume of organic phase (X1) (ml)	Concentration Of surfactant (X2) (% mg/V)	Amount of polymer (X3) (mg)	Particle size (Y1) (nm ± SD)*	PDI (Y2) (± SD)*	Zeta Potential (Y3) (MV± SD)*
Q1	1	10.00	1.00	100.00	86.65 ± 5.91	0.138 ± 0.030	- 12.73 ± 0.645
Q2	2	7.50	1.50	100.00	114.42 ± 19.03	0.178 ± 0.0075	- 12.6 ± 0.396
Q3	3	7.50	1.00	100.00	117.53 ± 14.97	0.051 ± 0.159	- 16 ± 0.426
Q4	4	7.50	1.50	100.00	148.72 ± 18.73	0.138 ± 0.006	- 17.2 ± 0.58
Q5	5	7.50	1.00	150.00	176.38 ± 19.31	0.028 ± 0.198	- 17.733 ± 0.66
Q6	6	7.50	0.50	100.00	90.17 ± 9.63	0.176 ± 0.034	- 17.266 ± 0.55
Q7	7	7.50	1.00	50.00	66.91 ± 7.14	0.159 ± 0.026	- 15.33 ± 0.475
Q8	8	5.00	0.50	100.00	161.11 ± 14.74	0.229 ±0.026	- 21.43 ± 0.49
Q9	9	7.50	1.00	100.00	115.93 ± 19.88	0.177 ± 0.0075	-12.3 ± 0.767
Q10	10	10.00	1.50	100.00	78.5 ± 4.65	0.171 ± 0.057	-10.45 ± 0.767
Q11	11	7.50	1.00	100.00	100.01 ± 3.08	0.166 ± 0.013	-13.166 ± 1.123
Q12	12	7.50	1.00	100.00	108.65 ± 17.76	0.123 ± 0.035	-14.766 ± 0.862
Q13	13	7.50	0.50	50.00	40.94 ± 9.51	0.116 ± 0.031	-16.74 ± 0.992
Q14	14	7.50	1.00	150.00	166.6 ± 8.88	0.214 ± 0.0043	-16.466 ± 0.377
Q15	15	7.50	1.50	150.00	172.96 ± 5.62	0.123 ± 0.010	-14.93 ± 0.293
Q16	16	5.00	1.00	50.00	87.97 ± 6.30	0.168 ± 0.027	-15.1 ± 0.9513
Q17	17	5.00	1.00	150.00	225.53 ± 6.30	0.366 ± 0.03	-18.633 ± 0.495
Q18	18	10.00	1.00	100.00	80.62 ± 15.14	0.16 ± 0.008	-15.466 ± 1.019
Q19	19	7.50	1.00	50.00	61.73 ± 12.55	0.195 ± 0.050	-16.166 ± 0.538
Q20	20	7.50	0.50	100.00	88.75 ± 21.18	0.149 ± 0.04	-22.93 ± 0.79
Q21	21	7.50	1.50	50.00	59.29 ± 6.92	0.298 ± 0.0057	- 11.243 ± 1.138
Q22	22	10.00	1.00	150.00	119.31 ± 9.47	0.078 ± 0.007	-11.466 ± 0.940
Q23	23	5.00	1.00	100.00	169.77 ± 11.64	0.201 ± 0.022	- 17.3 ± 0.582
Q24	24	7.50	1.00	100.00	100.42 ±7.39	0.183 ± 0.018	-14.933 ± 0.380
Q25	25	5.00	1.50	100.00	181.87 ± 4.95	0.180 ± 0.013	-16 ± 0.285
Q26	26	7.50	0.50	150.00	129.64 ± 4.11	0.338 ± 0.33	-16.8 ± 0.53
Q27	27	5.00	1.00	100.00	152.61 ± 6.1	0.163 ± 0.017	-20.7 ± 0.714
Q28	28	10.00	1.00	50.00	34.56 ± 7.83	0.297 ± 0.02	-13 ± 0.846
Q29	29	10.00	0.50	100.00	64.75 ± 0.89	0.097 ± 0.001	-16.9 ± 0.949

Data are shown as mean ± standard deviation

Particle size effects of formulation factors (Y1)

The particle size varied from 34.56 ±7.83 nm to 225.53 ± 6.30 nm According to Figure 2, the amount of Eudragit L- l00 had a major and positive influence on particle size. Results show that the particle size increased because the amount of polymer increased. the identical effect was observed with increasing Pluronic (F-68) concentration,. In contrast to those findings, the volume of organic solvent had an opposite effect. Increasing the volume of organic solvent resulted within the formation of smaller particles.

Formulation factors' effects on PdI (Y2)

The polydispersity indices ranged from 0.028 ± 0.19 to 0.338 ± 0.33, were modest, and exhibited minimal variation between the several samples. Figure 2 provides the PdI response surfaces. PdI rose as Eudragit L-100 was used more and more. Additionally, Pluronic (F-68) concentration and organic solvent volume had a favorable effect on PdI.

Zeta potential effects of formulation factors (Y3)

The fact that Eudragit L-100 is an anionic copolymer based on methacrylic acid and ethyl acrylates may be the reason why the electrical charge was negative for all samples. available on the nanoparticles' surface. Figure 3 depicts the impact of the concentration of Pluronic (F-68) and Eudragit L100 on the zeta potential, which varied from -22.93 ± 0.79 mV to -11.24 ± 1.138 mV. According to this number, adding Eudragit L-100 led marginally raises the zeta potential. The surface charge decreased as the concentration of pluronic (F-68) increased. On the other hand, zeta potential absolute values dropped as organic solvent volume increased.

TABLE 4 : Particle Size and PDI and linear parameter for zeta potential -quadratic-parameter values observed

Response	Adjusted R2	Predicted R2	Adequate precision	Lack of fit F-value	Model F-value	R-Squared
Particle size (Y1)	0.9576	0.9256	33.752	0.93	71.24.	0.9712
PDI (Y2)	0.89067	0.8237	20.702	0.91	26.33	0.9252
Zeta potential (Y3)	0.5648	0.3554	8.64	0.99	5.04	0.7047

Optimization and validation

QU-nanoparticles were generated under the software's recommended settings to test the model's predictive capacity. The program anticipated response range values based on these conditions. Table V shows the reactions' expected and actual experimental values. It was discovered from the analysis of the quadratic equation, contour plots, and three-dimensional response surface graphs produced by the Design-Expert software that the volume of the organic phase, concentration of surfactant, and amount of polymer have a significant impact on the particle size, PDI, and zeta potential of nanoparticles. Utilizing the numerical point prediction approach of the Design Expert software®, the optimal formulation of QU-NPs was chosen based on the criteria to achieve smallest particle size and maximum PDI and zeta potential. The selected optimized formulation for QU-NPs contained a 5.46 ml volume of ethanol,50 mg of polymer and 0.5% w/v of surfactant concentration with the value of desirability of 0.850. The experimentally average obtained values for the three samples of particle size (71.64 nm) ,PDI (0.235) and zeta potential (-17.03) of QU-NPs were found in agreement with the predicted value of particle size (74.39 nm) and PDI(0.0784) and zeta potential (-18.837) generated by Design Expert software® 12

DISCUSSION

Experimental design analysis. Fitting the model

The most helpful information for fitting the model is provided by R2 and Q2. The model's appropriateness and whether the proper model type was initially selected are determined by the model's validity. [25,31,32] The R2 is high, which indicates that the model fits and predicts all responses, including particle size, PdI, and zeta potential. All Q2 values are more than 0.5, with the exception of the zeta potential response. For each of the three replies, model validity and repeatability are more than 0.25 and 0.5, respectively.. Overall, the findings indicate that the selected model well characterized the connection between the formulation components and the responses, indicating a robust and dependable model with excellent predictive potential.

To ascertain whether the variance in the results is due to variations in the formulation components or to experimental mistakes, the analysis of variance (ANOVA) is utilized [21]. When p 0.05 is reached, the results are deemed significant.

And the test is passed. The significance of the regression model is assessed by one of the two F-tests in ANOVA. The model error and replicate error are contrasted in the lack of fit test. The less inaccurate and poorly fitting the model is, the less error there is in the model. This test is met when $p > 0.05$, and the results are deemed non-significant [31].The model accurately characterized the data since the model's p-values were less than 0.05 and those indicating lack of fit were higher than 0.05.

Particle size effects of formulation factors (Y1)

The circulation half-life, cellular absorption, and bio distribution of nanoscale drug delivery systems are all influenced by particle size [32]. Smaller particles may be taken up to a greater degree than larger ones because cellular uptake is size dependant [33]. The particle size has an impact on the drug's release kinetics. The higher the release rate, the smaller the particle size [40].

The number of polymer chains per unit volume of organic solvent and the viscosity of the organic phase, may be used to explain the influence of amount of polymer on particle size [41]. The viscosity of the organic solution rose as the amount of polymer was increased. A lower net shear stress is associated with a higher viscosity, resulting in the generation of bigger droplets. In addition, higher viscosity slows the passage of the organic solvent into the aqueous phase, resulting in bigger droplets, which in turn produce larger nanoparticles [5].

Higher polymer concentrations, on the other hand, enhance interactions between polymers resulting in more polymer chains remaining linked during solvent diffusion into the aqueous medium [41].

Pluronic (F-68) can be positioned at the organic-aqueous interface to reduce interfacial tension and hence increase net shear stress. This would actually encourage the production of tiny particles. Still, raising the Poluronic (F-68) concentration increased the aqueous phase's viscosity, and therefore the particles' mean diameter rose as a result of reduced shear stress [36].

On the other hand, other research suggests that increased Pluronic (F-68) concentrations stimulate particle coalescence, resulting in bigger nanoparticles [4]. According to the literature, a small amount of Pluronic (F-68) stays attached to the nanoparticles because it forms an interconnected network with Eudragit at the surface [43]. The proposed process includes Pluronic (F-68) and Eudragit L100 molecules interpenetrating during nanoparticle formation, notably during the evaporation of the organic solvent. The hydrophobic portions of Pluronic (F-68) stay entrapped in the polymeric matrix after entering the organic solution [1]. As a result, residual Pluronic (F-68) might contribute to an increase in particle size at higher concentrations. Despite the fact that these findings contradict those reported by the majority of writers [1,40,42], They are consistent with prior findings [4,38] published by other organizations.

When the volume of organic solvent was increased, smaller particles were generated, according to the results. The larger the stirring speed, which impacts the viscosity of the dispersion, the smaller the resultant net shear stress [42]. The aqueous phase of the organic solvent is accelerated in rapid diffusion at the same time [5].

TABLE 5: characteristics of the QU-nanoparticles: predicted and experimental values

Response	Target	Predicted value		Expected value	Experimental value
		lower limit	upper limit		
Y1 Particle size (nm)	minimize	34.5667	225.533	74.39	71.64
Y2 PdI	minimize	0.07876	0.366667	0.081	0.235
Y3 Zeta potential (mV)	maximize	-21.4333	-11.2433	-18.83	-17.03

Effects of formulation factors on PdI (Y2)

An essential characteristic known as PdI is utilized to define the diversity in particle size within a population of particles. A multimodal distribution is most often found in the size of a population of particles. When PdI is almost 1, a wide variety of sizes is possible. The preferred value is often one that approaches 0 [21].

It appears that the quantity of polymer is the component affecting PdI that is least significant. One may argue that a higher Pluronic (F-68) content and amount of organic solvent would encourage the development of significantly more homogeneous nanoparticle samples.

Effects of formulation factors on zeta potential (Y3)

The zeta potential, sometimes referred to as the electrostatic potential, is a fundamental property that provides essential information on colloidal dispersion stability [43]. The electric charge on the surface of the nanoparticles causes it. The zeta potential of nanoparticles with a zeta potential of -10 mV to +10 mV is regarded reasonably neutral [5]. A zeta potential of less than -30 mV or greater than +30 mV,on the other hand, indicates a fairly steady dispersion [46]. The repulsive interactions between similarly charged particles prevent aggregation and promote stability at higher zeta potential levels [34].

Eudragit nanoparticles have a surface charge that is mostly negatively charged. mV in the absence of any pluronic (F-68). This is because, as already mentioned, Eudragit L-100 is an anionic copolymer. Despite repeated washings, the non-ionic stabiliser pluronic (F-68) leaves a protective coating on the surface of nanoparticles. [3,6]. The decrease in negative zeta potential values with increasing pluronic (F-68) concentration is thought to be due to the pluronic (F-68) coating of the nanoparticles shielding Eudragit's surface charge.

The production of tiny nanoparticles is aided by increasing the amount of organic solvent. Particle size, on the other hand, is directly proportional to surface charge.

CONCLUSIONS

This work successfully used a nanoprecipitation approach to create QU-loaded polymeric nanoparticles of the desired size. Its goal was to see how three formulation parameters affected particle size, PdI, and zeta potential. In order to investigate the impacts of the variables and improve the manufacturing process parameters, An experiment was conducted using the Box-Behnken design.

The amount of polymer had a substantial influence on all of the tested responses, especially nanoparticle size, according to the findings. An optimal formulation was established and created based on these findings. The best conditions for the creation of QU-nanoparticles were found to be a smaller amount of Eudragit L-100 combined with a lower pluronic concentration and volume of organic solvent.

Finally, It was successful to produce QU-nanoparticles with ideal characteristics using a Box-Behnken experimental strategy.

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