A R DIGITECH
International Journal Of Engineering, Education And Technology (ARDIJEET)
www.ardigitech.in ISSN 2320-883X,VOLUME 11 ISSUE 01 27/03/2023

OPTIMIZATION AND SELECTION OF DIFFERENT BATCHES TRANSETHOSOMAL FORMULATION EXCIPIENTS AND PROCESS VARIABLES

Authors: Machale Manjunath,, Kiran Kumar Gande[2] and Vitthal Gajananrao kuchake[3]
[1]*Research Scholar Sunrise University, Alwar, Rajasthan, India*
[2] Vice President- Regulatory Affairs Leading Pharma, LLC, 3 Oak Road, Fairfield, NJ-07004, USA
[3]*Research Guide Sunrise University, Alwar, Rajasthan, India*

Abstract:

The main aim of this study was to formulate and evaluate the Curcumin longa loaded transethosomes and conducted pre-formulation studies (compatibility study FTIR), solubility studies, melting point and determination of lambda max. Characterization Curcumin longa loaded transethosomes are TEM analysis, Particle size, Entrapment efficacy, Zeta potential, Drug content and In vitro dissolution studies. Post-evaluation studies for Curcumin longa L loaded transethosomal gel was conducted FTIR, DSC, Drug content and In vitro diffusion studies, kinetic studies and to improve patient compliance. According to optimization method (Box Behnke design) 15 formulation of Curcumin longa loaded transethosomes was developed by using Ethanol, edge activator and soya Lecithin liquid further from design expert provide optimized formulation then to that optimized Curcumin longa loaded transethosomes was developed into gel.

Key words: Transethosomal**,** Curcumin longa, Box Behnke design)

Introduction: Herbal Medicine [1, 2, 3, 4]

Natural active ingredients found in medicinal plants have the power to cure disease and reduce suffering. It is commonly known that the majority of underdeveloped countries employ traditional medicines and medicinal plants as therapeutic agents to preserve good health. The World Health Organisation estimates that in impoverished countries, traditional healers treat 80% of the population largely with herbal plant medicines. The plant's phytochemicals may be the source of its anti-oxidant, antibacterial, and antipyretic qualities. Since ancient times, people all around the world—including those who practise traditional medicine—have used herbs, which are believed to be non-toxic, to treat a variety of illnesses. Neither the general public nor professional groups in traditional medicine have accepted the possibility of herb poisoning, with several documented incidents of toxicity caused by their usage. More and more people are turning to medicinal plants as a source material for pharmaceuticals. India, also referred to as the Botanical Garden of the World, is believed to be the world's top country in the production of medicinal plants. Traditional medical systems like Ayurveda, Sidha and Unani have been using medicinal herbs in one way or another for thousands of years. On Earth, there are over 3.6 lakh different types of medicinal plants, with 1.4 lakh of them species found in India. A recent analysis found that almost 70,000 plants are used in traditional medicinal systems. All around the planet, our ancestors used plants as their main source of healing. When modern western medicine gained popularity, herbal therapy was initially less widespread in many cultures, as it was believed that synthetic chemicals were the most efficient way of healing sickness. A search for a healthier way of life has led to an increase in interest in the medicinal properties of herbs among people. Even in the West, natural products are now widely available, and herbalism is rising back to popularity in a society where people are becoming more medical and ecological-conscious. Herbal remedies can help prevent many of the unwanted side effects of modern drugs. There has been a clear turn

back towards traditional healthcare systems in an attempt to provide better care. In the future, people everywhere will favour receiving care from traditional medical systems. This is because, despite the fact that modern medicine has many established benefits, several disadvantages have limited its potential in the future. Due to the limitations of modern medicine, researchers are searching for substitutes, particularly in traditional and ancient medicine.

1.1 Traditional medicine [5, 6]

The body of medical knowledge that has developed over many generations within a community or among a population is known as traditional medicine. It involves medical professionals— both specialized and non-specialized—who use a system of diagnosis and treatment and who have predetermined criteria for different illnesses and symptoms. With their cultural differences, traditional medical systems all aim to achieve complete balance and harmony in the body, mind, and spirit. After several modifications during its long existence, it continues to be the main source of medical treatment for an important portion of the country's population. Many Asian nations, including China, India, Japan, and Pakistan, continue to value traditional medicine. The oldest known medical products are plants used for medicinal purposes. Their significance is still increasing.

1.1.1 Ayurveda [7]

One of the most well-known ancient medical systems that survived and grown throughout thousands of years is Ayurveda. This system is going to survive for years to come because of the deep understanding of nature-based medicine, the link between the composition and functions of the human body and nature, and the components of the universe that operate in unity and impact living things. The scholars, practitioners, and industry specialists who have the responsibility of preserving traditional medical systems (TSMs) and promoting their growth in the future have an infinite number of pathways to explore. It is among the most well- known medical systems in the entire globe. The foundation of Ayurveda is the idea that everything in the universe is made up of five fundamental elements: space, air, energy, liquid, and solid. Within the human body, they take on limited forms such as pitta (energy and liquid), kapha (liquid and solid), and vata (space and air). The three pillars of life, or tridosha, are vata, pitta, and kapha together. An imbalance between these will result in a disease.

1.1.2 Unani system of medicine [8]

Hippocrates, a well-known physician and philosopher who lived from 460 to 366 BC, introduced the Unani medical system to Greece. Hippocrates established the "humoral theory" of medicine, defining the wet and dry properties of the several humours that make up the human body. The Unani medical system was introduced to India by the Arabs, and it became more powerful when several Unani intellectuals and doctors migrated to India during the Mongol invasion of Persia. Since then, this medical system has established itself strongly in India and

is approved by the government for financing for both clinical practice and research. Plant-based formulations such as tinctures, oils, powders, and ointments are employed in medical practices.

1.1.3 Homoeopathic system of medicine [9]

Homoeopathic medical system German physician and chemist Samuel Hahnemann created homoeopathy in the eighteenth century, making it a more modern medical system than other traditional ones. He

suggested treating an illness by targeting its root cause. The law of similarities, which states that "like cures like," was proposed by him. He proved how cinchona may cause malaria symptoms using this theory. He recorded all of his research in a book titled "The Organon of Medicine." The homoeopathic approach fails to establish a course of therapy; alternatively, the choice of medication is based on the patient's clinical condition and symptoms. The core of this concept is the idea of proving and show. The symptoms produced by varying dosages of drug extracts are documented in a healthy individual known as prover; if physical, mental, and emotional alterations of prover are clearly taken into consideration. As a result, the patient with these symptoms is also experiencing comparable symptoms, and as a result, the same kind of extract is being administered for therapy. Arnica, Belladona, Chamomile, Colchicum, Hyocyamus, Ipecacuhna, Lycopodium, Opium, Ergot, Nux-vomica, and other medicinal herbs are among those utilized in the homoeopathic method.

1.1.4 The Siddha system of medicine

Since the human body is made up of the five components of the universe, or the pancha mahabhootas, the Siddha medical system is founded on a similar theory to Ayurveda. In addition to these parts, the Siddha system holds that 96 variables influence an individual's physical, moral, and physiological well-being. These ninety-six variables include speech, perception, pulse diagnosis, and more. With the help of minerals, metals, and, to a lesser extent, some plant items, perception is frequently employed as a factor for the treatment of psychosomatic disorders. The Siddha method makes use of several powdered plant and mineral preparations that are made using a variety of processes, including as the calcinations.

1.1.5 Yoga [10,11,12]

Yoga had its ancient roots in India. It provides treatments, diagnosis based on an individual's pulse and analysis of their Tridosha condition, and lifestyle management recommendations for achieving peace of mind and better health. Yoga positions, or poses, are used to treat a wide range of medical and non-medical diseases, both mental and physical.

Aim and Objectives:

To Formulate and Evaluate transethosomal gel that incorporates a herbal extract of Curcumin extract to optimize localized drug delivery and enhance analgesic efficacy.

✓ To optimized formulation of the transethosomes that integrates a specific herbal extract recognized for its analgesic properties by using the Box Bhenken Design.

Determination of absorption maxima of *Curcumin Longa*: A precisely measured 100 mg of drug

The current study utilized a Box–Behnken design to assess the interactions and effects of formulation-independent parameters at varying levels on three significant quality attributes: particle size(Y1), entrapment efficiency(Y2) and PDI(Y3). The experimental results of the Box–Behnken design are summarized in The relationship between various independent variables such as soya lecithin (ml), Ethanol (%), and tween 80 (ml), and dependent variables such as particle size(nm), % EE and PDI is illustrated in the 3D graphs. The quadratic model was found to be the most appropriate fit for all the responses under consideration. The statistical significance of the regression coefficients for the input factors was assessed using the corresponding *p*-value, which was calculated via analysis of variance (ANOVA)

Figure no. 1: Transethosomal Formulation work

Statistical analysis of the data and optimization through Box-Behnken design (Design Expert, Version 13):

Experimental design and surface technique are significant tools for identifying diverse factors influencing responses through a short number of trials. For experimental purposes, we used Box-Bahnken design (Design Expert, Version 13). Three levels were chosen for each element, based on the results of the single factor experiment and the ability to prepare formulations at the highest and minimum values. Design Expert, Version 13 was used to optimise all Vesicular formulations by identifying dependent and independent factors. The acquired answers were fitted into a variety of mathematical models, including linear, two-factor interactions (2FI), and quadratic models. On the basis of lower values of standard deviation (SD) and coefficient of variation (%CV), as well as high values of correlation coefficient (R^2), predicted R^2 and adjusted R^2 the best fit form was decided.

To assess the influence of independent factors on each response, multiple regression analysis was performed on the received responses, yielding a second order polynomial equation. The size of the coefficients determines whether the polynomial equation is positive or negative. Higher coefficient values indicate significant model terms, whereas lower coefficient values signal insignificant model components. A positive sign in a polynomial equation implies that increasing the level of one variable generates an increase in that specific response, whereas a negative sign suggests that increasing the level of one variable causes a reduction in the corresponding response. The ANOVA test was performed to determine the significance of the model and its terms. If the p-value (significant probability value) is less than 0.05, the model is considered significant. The 3D-response surface plots were utilized to reveal the main and interaction effect of independent variables on the individual responses.

Fitting of data to the model:

The observed responses for all formulations were simultaneously fitted to various mathematical models using Design-Expert® software to find the best fit model. The comparative values of SD, R^2, adjusted R^2, predicted R^2, CV will be shown.

Optimization plan for *Curcumin Longa* loaded Transethosomes:

The optimization of *Curcumin Longa* loaded transethosomes was performed. A 3^3 randomized factorial design used within the framework of Response Surface Methodology used in this study and three factors were evaluated, each at three levels.

Table no. 1: Design of Experiment by using BBD

Formulation Code	**Independent Variables**			**Dependent variable**		
	Factor 1	**Factor 2**	**Factor 3**	**Response 1**	**Response 2**	**Response 3**
	Soya Lecithin (A)	Ethanol (B)	Edge activator (C)	particle size (Y1)	Entrapment Efficiency (Y2)	PDI (Y3)
	ml	%	ml	nm	percentage	
1	1	40	0.75	344.3	61.32	0.417
2	1.5	40	0.5	298.7	55.4	0.433
3	1.5	40	1	270.2	65.11	0.461
4	1	10	0.75	337.6	66.71	0.357
5	1	25	0.5	321.7	63.21	0437
6	2	40	0.5	397.9	76.31	0.277
7	2	25	1	370.7	79.85	0.232
8	2	25	0.5	361.6	69.4	0.348
9	**1.5**	**10**	**0.75**	**270.2**	**68.70**	**0.352**
10	1.5	10	1	278.3	58.3	0.300
11	2	10	0.75	399.7	80.11	0.202
12	1	25	1	300.9	57.7	0.434
13	1.5	25	0.75	326.9	71.88	0.236
14	1.5	25	0.75	329.1	71.07	0.223
15	1.5	25	0.75	326.8	71.77	0.253

Effect of Independent variable on Particle size (Y1):

Quadratic polynomial equation:

$$Y1 = 327.60 + 28.17A + 3.16B - 4.01C - 2.13AB + 7.7AC - 9.15BC + 50.82A^2 - 8.55B^2 - 39.70C^2$$

Y1 is Particle size, A= Soya lecithin, B =Ethanol and C =Tween 80

Here, Y1 represents the Particle size. From the equation, it is clear that concentration of Soya lecithin has a positive effect on the Particle size(the concentration of soya lecithin increases, the particle size increases, especially at lower concentrations) & the percentage of Ethanol also has a positive effect **(**higher ethanol percentages, the particle size decreases more significantly). so, it is observed that the Concentration of edge

activator (tween 80) has negative effect on particle size (the concentration of edge activator increases, the particle size decreases).

Table no. 2: The ANOVA results for the data of the Particle size

Response 1: particle size

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	24063.64	9	2673.74	282.20	< 0.0001	significant
A-Soya Lecithin	6350.65	1	6350.65	670.29	< 0.0001	
B-Ethanol	80.01	1	80.01	8.44	0.0336	
C-Edge activator	128.80	1	128.80	13.59	0.0142	
AB	18.06	1	18.06	1.91	0.2259	
AC	223.50	1	223.50	23.59	0.0046	
BC	334.89	1	334.89	35.35	0.0019	
A^2	9537.90	1	9537.90	1006.69	< 0.0001	
B^2	269.92	1	269.92	28.49	0.0031	
C^2	5819.41	1	5819.41	614.22	< 0.0001	
Residual	47.37	5	9.47			
Cor Total	24111.01	14				

The analysis reveals that the individual concentrations of soya lecithin (A), ethanol (B), and edge activator (C) each have a significant effect on particle size. Among these, soya lecithin exerts the strongest influence, as indicated by its high F-value and low p-value. This suggests that changes in soya lecithin concentration can markedly alter particle size. Additionally, two of the interaction terms, AC (soya lecithin * edge activator) and BC (ethanol * edge activator), are also statistically significant, highlighting that the combined effect of these pairs of variables meaningfully impacts particle size. However, the interaction between soya lecithin and ethanol (AB) does not significantly affect particle size, indicating that these two factors operate more independently in this context. The quadratic terms for soya lecithin (\(A^2\)), ethanol (\(B^2\)), and edge activator (\(C^2\)) are all highly significant, suggesting non-linear relationships between these factors and particle size. This implies that beyond simple linear changes, increases in each factor at higher concentrations can lead to complex effects, further influencing the particle size in a non-linear manner.

- **Response surface plot of Particle size:**

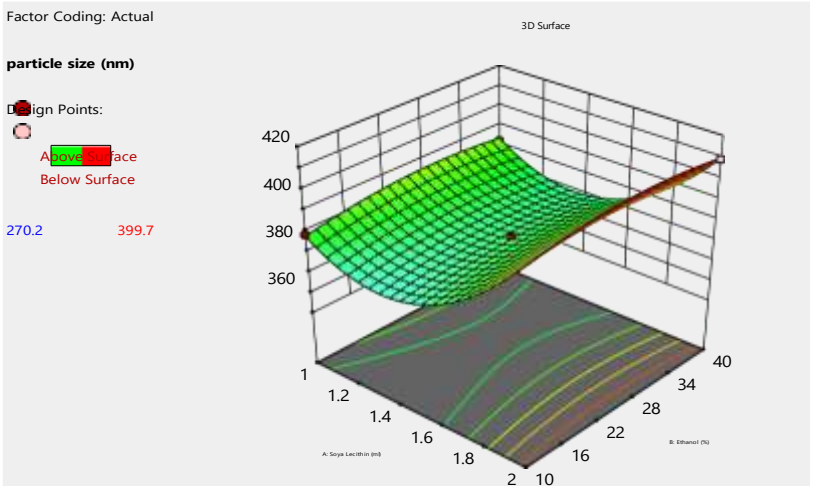

Figure no. 2: 3D Graph of influence of Concentration of soya lecithin and ethanol on particle size.

The surface plot shows that as soya lecithin concentration (A) and ethanol percentage (B) increase, the particle size also increases. Soya lecithin has a stronger effect on particle size, with a noticeable increase as its concentration rises. Ethanol also contributes to particle size growth, though more gradually. The upward slope of the plot suggests an interaction between the two factors, where higher levels of both lead to larger particle sizes.

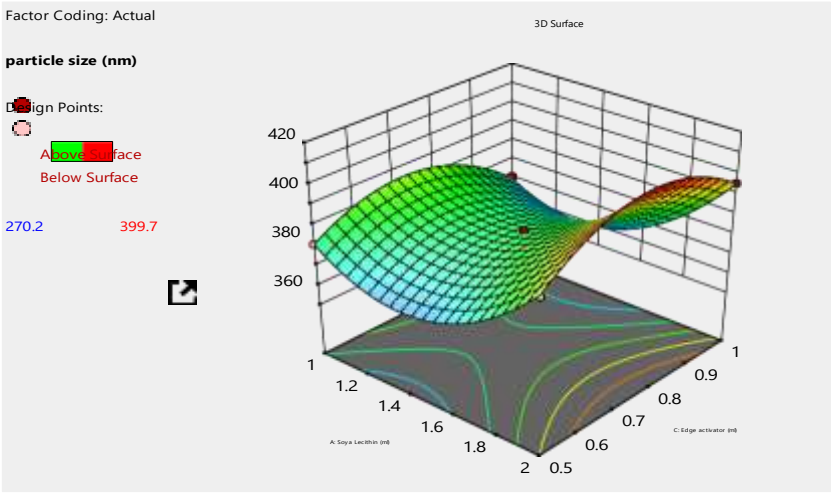

Figure no. 3: 3D Graph of influence of Concentration of Soya lecithin & Edge activator on particle size.

Soya Lecithin and **Edge Activator** are commonly used in drug formulation to stabilize particles or influence particle size. In nanoparticle formulation, altering the concentrations of these components can influence the size of the particles formed, which affects the release and stability of the drug.A smaller particle size often enhances drug absorption due to a larger surface area, while larger particles may have slower absorption rates. This graph can help optimize the particle size by adjusting the concentrations of the components.The curved nature of the plot suggests non-linear interactions between soya lecithin and the edge activator, meaning changes in particle size are not proportional to changes in either of the two factors individually.

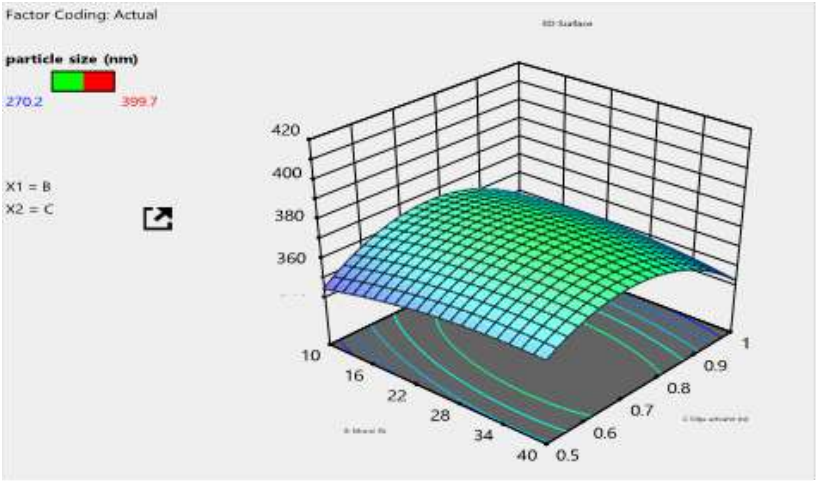

Figure no. 4: 3D Graph of influence of Ethanol & Edge activator on particle size.

Ethanol (%) and **Edge Activator** play crucial roles in particle formation. Ethanol can impact the solvent polarity and particle formation dynamics, while edge activators, often surfactants, help stabilize particles by reducing surface tension.

The graph's curvature indicates non-linear interactions, meaning the effect on particle size isn't simply additive for changes in ethanol and edge activator alone. For example, increasing ethanol concentration in the presence of specific edge activator levels may yield larger particles. Smaller particle sizes are often preferred in pharmaceutical formulations for enhanced bioavailability. This graph helps identify the optimal ethanol and edge activator levels for achieving the desired particle size.

5.2.2 Effect of Independent variable on Entrapment efficiency: Quadratic polynomial equation:

$$Y2 = 71.57 + 7.67A - 1.94B + 0.5500C + 0.3975AB + 3.99AC + 4.99BC + 2.62A^2 - 3.08B^2 - 6.65C^2$$

Here, Y2 represents the Entrapment efficiency. From the equation, it is clear that concentration of Soya lecithin has a positive effect on the Entrapment efficiency (higher soya lecithin concentration likely enhances the entrapment efficiency) & the percentage of ethanol also has a negative effect **(**increasing Ethanol concentration decreases EE). so, it is observed that the concentration of edge activator has positive effect on entrapment efficiency.

Table no. 3: The ANOVA results for the data of the Entrapment Efficiency Response 2: Entrapment Efficiency

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	827.72	9	91.97	89.20	< 0.0001	significant
A-Soya Lecithin	402.29	1	402.29	390.15	< 0.0001	
B-Ethanol	30.15	1	30.15	29.24	0.0029	
C-Edge activator	2.42	1	2.42	2.35	0.1861	
AB	0.6320	1	0.6320	0.6130	0.4691	
AC	63.68	1	63.68	61.76	0.0005	
BC	99.60	1	99.60	96.60	0.0002	
A^2	25.34	1	25.34	24.57	0.0043	
B^2	35.04	1	35.04	33.98	0.0021	
C^2	163.43	1	163.43	158.50	< 0.0001	
Residual	5.16	5	1.03			
Cor Total	832.88	14				

The analysis indicates that **Soya Lecithin (A)** has the largest individual impact on entrapment efficiency, making it a critical factor in the formulation. **Ethanol (B)** also significantly influences entrapment efficiency, though to a lesser degree than soya lecithin. In contrast, the **Edge Activator (C)** alone does not show a statistically significant effect on entrapment efficiency; however, when combined with other factors, it demonstrates a notable impact. Specifically, the **AC (Soya Lecithin × Edge Activator)**and **BC (Ethanol × Edge Activator)** interactions are significant, indicating that the edge activator's role becomes important in combination with either soya lecithin or ethanol. Furthermore, the **C^2 (Edge Activator squared)** quadratic term is highly significant, suggesting a non-linear effect of edge activator concentration on entrapment efficiency, likely contributing to complex interactions within the system. This underscores the importance of optimizing edge activator levels alongside other factors to achieve optimal entrapment efficiency.

- **Response surface plot of Entrapment Efficiency:**

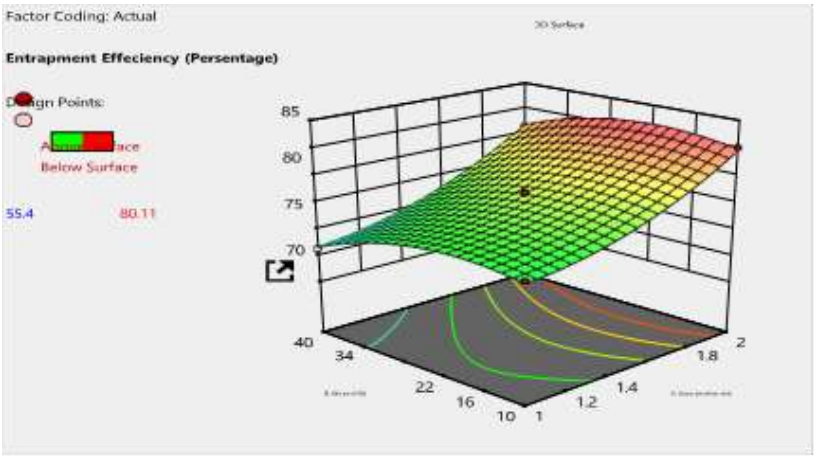

Figure no.5: 3D Graph of influence of soya lecithin and Ethanol on Entrapment efficiency

Positive Correlation of Soya Lecithin and Entrapment Efficiency: As the concentration of soya lecithin increases, the entrapment efficiency also increases. This is likely because lecithin improves the structural integrity of the formulation, allowing it to encapsulate more of the target substance. Higher ethanol percentages also tend to increase entrapment efficiency, although its effect appears less significant than that of soya lecithin. Ethanol can change the fluidity and permeability of lecithin structures, enhancing the encapsulation process, but only to a certain extent.

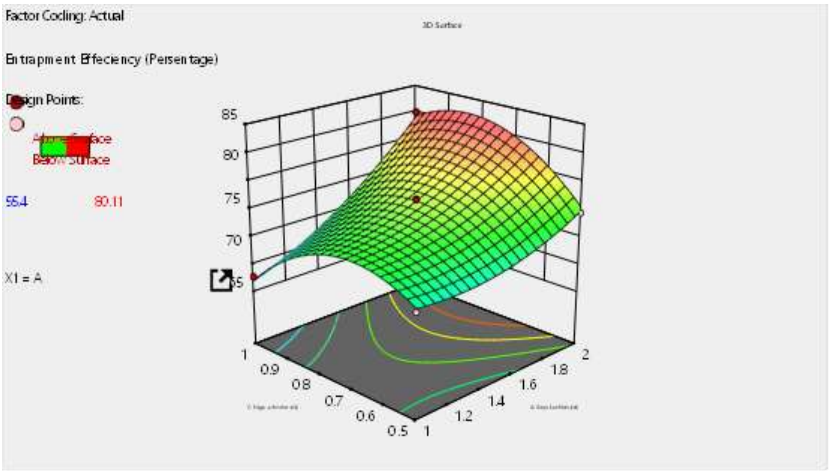

Figure no. 6: 3D Graph of influence of soya lecithin and edge activator on Entrapment efficiency

This 3D surface plot illustrates the relationship between entrapment efficiency (percentage) and two variables: span length (A) and edge distance (C), with a third factor (B) held constant at a value of 25. The z-axis shows entrapment efficiency, color-coded from blue (low efficiency, around 55%) to red (high efficiency, up to about 80%). The contour plot at the base provides a top-down view, with colors and lines matching the surface to help visualize efficiency across different combinations of span length and edge distance. The design points marked as "Above Surface" and "Below Surface" represent specific measured or simulated data points relative to the predicted surface. Generally, the plot indicates that entrapment efficiency increases with higher span length and lower edge distance, which can be used to guide parameter adjustments for optimal efficiency under the fixed conditions. This 3D surface plot illustrates the relationship between entrapment efficiency (percentage) and two variables: span length (A) and edge distance (C), with a third factor (B) held constant at a value of 25. The z-axis shows entrapment efficiency, color-coded from blue (low efficiency, around 55%) to red (high efficiency, up to about 80%). The contour plot at the base provides a top-down view, with colors and lines matching the surface to help visualize efficiency across different combinations of span length and edge distance. The design points marked as "Above Surface" and "Below Surface" represent specific measured or simulated data points relative to the predicted surface. Generally, the plot indicates that entrapment efficiency increases with higher span length and lower edge distance, which can be used to guide parameter adjustments for optimal efficiency under the fixed conditions.

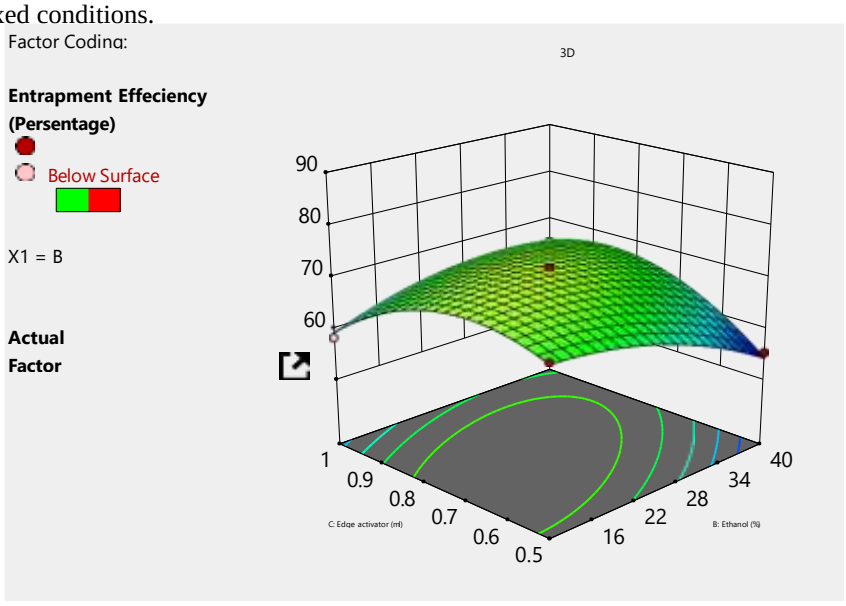

Figure no. 7: 3D Graph of influence of ethanol and edge activator on Entrapment efficiency

This 3D surface plot illustrates how entrapment efficiency varies with two variables, B and C, while a third variable, A, is held constant at 1.5. Efficiency peaks in the yellow-green region of the plot, suggesting optimal conditions occur at moderate to high values of B and mid-range values of C. The color gradient, from blue (low efficiency) to yellow (high efficiency), shows how efficiency changes across the tested parameter space. Design points above and below the surface represent actual data points, highlighting the model's accuracy in predicting efficiency. This analysis is useful for optimizing conditions to maximize entrapment efficiency in applications like chemical and pharmaceutical formulations. This 3D surface plot

illustrates how entrapment efficiency varies with two variables, B and C, while a third variable, A, is held constant at 1.5. Efficiency peaks in the yellow-green region of the plot, suggesting optimal conditions occur at moderate to high values of B and mid-range values of C. The color gradient, from blue (low efficiency) to yellow (high efficiency), shows how efficiency changes across the tested parameter space. Design points above and below the surface represent actual data points, highlighting the model's accuracy in predicting efficiency. This analysis is useful for optimizing conditions to maximize entrapment efficiency in applications like chemical and pharmaceutical formulations.

5.2.3 Effect of Independent variable on Poly dispersity Index:

Quadratic polynomial equation:

$$Y3= 0.237-0.0732A+0.0471B-0.0179C+0.0038AB$$

$$0.0282AC+0.0200BC+0.0261A^2+0.0498B^2+0.0993C^2$$

Here, Y2 represents the Polydispersity index(PDI). From the equation, it is clear that concentration of Soya lecithin has a negative effect on the PDI (higher soya lecithin concentration decreases PDI, creates a more uniform particle size distribution) & the percentage of ethanol has a positive effect (increasing Ethanol concentration increases PDI

,gives broader PDI). so, it is observed that the concentration of edge activator has Negative effect on PDI (promoting a more uniform particle size distribution).

Table no. 4: The ANOVA results for the data of the PDI

Response no. 3: PDI

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	0.1120	9	0.0124	20.65	0.0019	significant
A-Soya Lecithin	0.0429	1	0.0429	71.21	0.0004	
B-Ethanol	0.0178	1	0.0178	29.47	0.0029	
C-Edge activator	0.0026	1	0.0026	4.24	0.0945	
AB	0.0001	1	0.0001	0.0933	0.7723	
AC	0.0032	1	0.0032	5.30	0.0697	
BC	0.0016	1	0.0016	2.65	0.1642	
A^2	0.0025	1	0.0025	4.17	0.0967	
B^2	0.0092	1	0.0092	15.21	0.0114	
C^2	0.0364	1	0.0364	60.44	0.0006	
Residual	0.0030	5	0.0006			
Cor Total	0.1150	14				

The ANOVA table shows that the model is statistically significant (p = 0.0019), indicating that the factors studied—soya lecithin (A), ethanol (B), and edge activator (Tween 80, C)— influence the response variable. Soya lecithin (p = 0.0004) and ethanol (p = 0.0029) have significant positive effects, while Tween 80's effect is not statistically significant (p = 0.0945). Among interaction terms, none are significant, though the soya lecithin and Tween 80 interaction (AC) is marginally close (p = 0.0697). Quadratic terms

for ethanol (p = 0.0114) and Tween 80 (p = 0.0006) are significant, indicating a strong curvilinear effect on the response.

- **Response surface plot of PDI:**

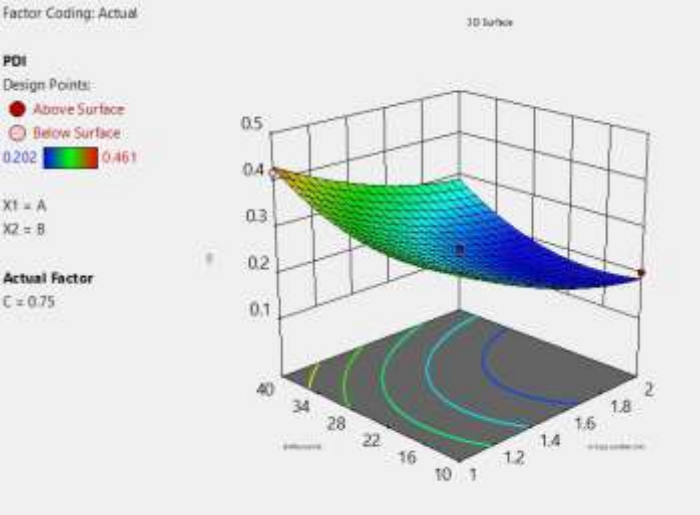

Figure no. 8: 3D Graph of influence of soya lecithin and Ethanol on PDI

This 3D plot illustrates how PDI (Polydispersity Index) is influenced by soya lecithin (A) and ethanol (B), with Tween 80 (C) fixed at 0.75. Higher soya lecithin and lower ethanol levels lead to lower PDI, as shown by the blue region on the surface. The curved surface and contour lines indicate an interaction between soya lecithin and ethanol, where the optimal conditions for minimizing PDI are at high soya lecithin and low ethanol concentrations.

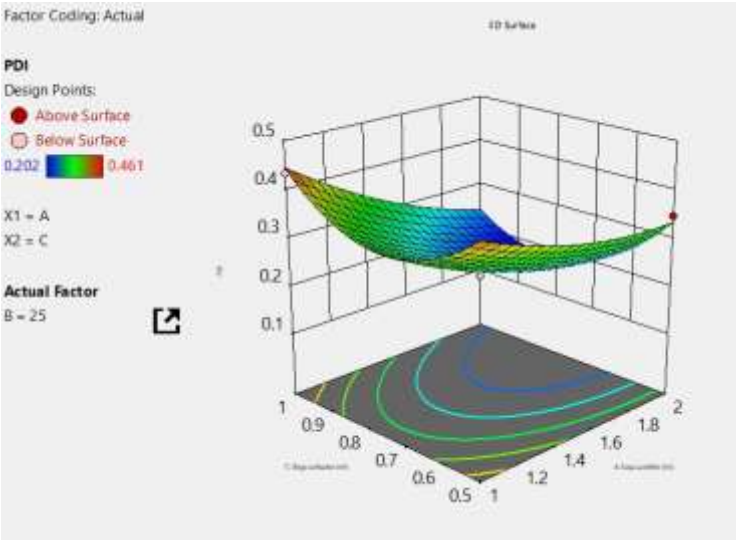

Figure no.9: 3D Graph of influence of soya lecithin and edge activator on PDI

This 3D plot illustrates the effect of soya lecithin (A) and edge activator (Tween 80, C) on the Polydispersity Index (PDI), with ethanol (B) fixed at 25%. The plot shows that higher concentrations of both soya lecithin and edge activator lead to a lower PDI, as seen in the blue region. The downward curvature of the surface indicates an interaction between A and C, where the optimal PDI reduction is achieved when both are at higher levels.

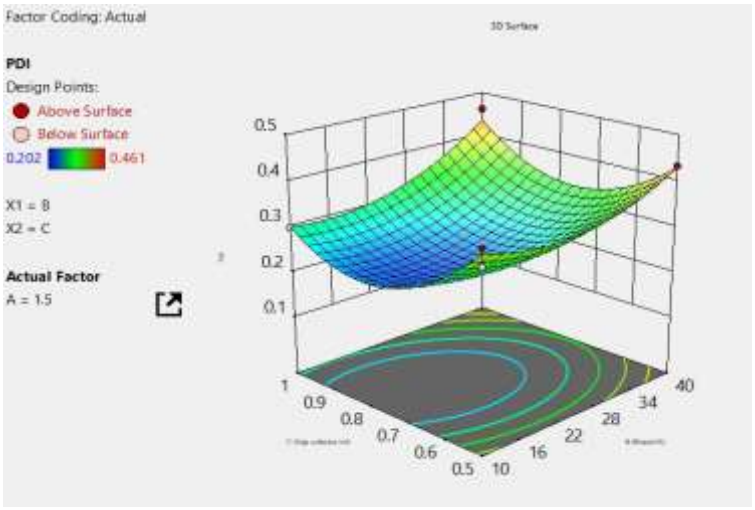

Figure no. 10: 3D Graph of influence of ethanol and edge activator on PDI

This 3D surface plot shows how the response variable, PDI (Polydispersity Index), changes with variations in Ethanol concentration (B) and Egg White concentration (C) when a third factor (A) is held constant at 1.5. The color gradient on the surface indicates PDI values, with blue for lower values and red for higher values. The contour plot below offers a top-down view, highlighting specific PDI levels across the range of B and C. Design points (red and black dots) mark where data was collected, with red indicating above-surface values and black below- surface values. This visualization helps understand how Ethanol and Egg White levels impact PDI, aiding in optimization or prediction.

Optimized batch:

Table no. 5: Optimized batch of transethosomes

Number	Soya Lecithi n	Ethan ol	Edge activat or	particl e size	Entrapment Efficiency	PDI	Desirabili ty	
1	*1.305*	*22.094*	*0.915*	302.449	65.277	0.299	1.000	
2	*1.500*	*10.000*	*1.000*	281.325	59.341	0.301	1.000	
3	***1.500***	***10.000***	***0.500***	**271.050**	**68.221**	**0.377**	**1.000**	Selecte d

Conclusion:

Optimization of the formulation was achieved through a Box-Behnken design, resulting in 15 experiments of the Curcumin-loaded transethosomes. An optimized formulation was selected based on entrapment efficiency and particle size. Characterization of the optimized Curcumin-loaded transethosomes demonstrated high entrapment efficiency (68.70%), stable zeta potential (-16.6 mV), and nanoscale particle size (270.2 nm). Transmission Electron Microscopy (TEM) revealed a spherical morphology, enhancing the potential for skin permeation. The gel formulation has favourable physicochemical features, facilitating long-term retention topically while also displaying considerable antibacterial activity against *Staphylococcus aureus*. In vitro dissolution and kinetic studies confirmed the sustained release of the drug via Korsmeyer-Peppas model, indicating a diffusion and erosion-controlled mechanism for drug release.

References:

1. Ajazuddin S. Saraf, Applications of novel drug delivery system for herbal formulations, Fitoterapia. 2010; 81: 680–689.
2. Junaid Khan, Amit Alexander, Ajazuddin, Swarnlata Saraf, Shailendra Sara, Recent advances and future prospects of phyto-phospholipid complexation technique for improving pharmacokinetic profile of plant actives, Journal of Controlled Release. 2013; 168: 50–60.
3. Surendra Tripathy, Dilip K Patel, Lipika Baro, et al., A review on phytosomes, their characterization, advancement & potential for transdermal application, journal of drug delivery & therapeutics. 2013;3(3):147-152.
4. P.K. Mukherjee, A. Wahile, Integrated Approaches towards drug development from Ayurveda and other Indian System of Medicine, Journal of Ethnopharmacology. 2006; 103:25-35.
5. Jagruti Patel, Rakesh Patel, Kapil Khambholja, Nirav Patel, An overview of phytosomes as an advanced herbal drug delivery system, Asian journal of pharmaceutical sciences. 2009; 4 (6):363-371.
6. D. Dubey, S. Shrivastava, S. Kapoor, et al., Phytosome: a novel dosage structure. 2007, http://www.pharmainfo.net/reviews/ phytosome-novel-dosage-structure.
7. E. Bombardelli, M. Spelta, Phospholipid-polyphenol complexes: A new concept in skin care ingredients. Cosm & Toil. 1991;106(3): 69-76.
8. M. Lampertico. Marena, Preliminary clinical development of silipide: A new complex of silybin in toxic liver disorders. Planta Med. 1991; 57:A124-A125.
9. Barzaghi N, Crema F, Gatti G, et al. Pharmacokinetic studies on IdB 1016. A silyliin-phosphariJylcholine complex, in healthy human subjects. Eur J Drug Metah PiwmKicDfcmci 1990; 15:333-338.
10. X. Yanyu, S. Yunmei, C. Zhipeng, et al. The preparation of silybin-phospholipid complex and the study on its pharmacokinetics in rats. Int. J. Pharm. 2006; 307: 77-82.