ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Formulation And Evaluation Of A Phytoconstituent In To A Tablet Dosage Form.

Gupta SC[1], and Phatak AA[2]*.

[1]Department of Pharmaceutics, Progressive Education Society's Modern College of Pharmacy, Nigdi, Pune-411044, Maharashtra, India.
[2]Department of Pharmaceutics, Progressive Education Society's Modern College of Pharmacy, Nigdi, Pune-411044, Maharashtra, India.

ABSTRACT

The goal of the current study was to create a new vesicular formulation that would target a specific drug, enhance body resistance time, and improve bioavailability by raising aqueous solubility. By using a solid dispersion technique, the phytoconstituent was transformed into a nanocarrier and then transformed once more into a tablet dosage form. In order to ensure that the ingredient is of a particular quality and to reduce further risk, preformulation studies and validation were employed. A 2^2 factorial design was employed to study the effect of independent variables X_1- Different concentration of carrier (100-200mg), X_2-Different concentration of polymer (50-100mg) on dependent variables Y_1-Disintegration time (sec),Y_2-Friability (%), Y_3-Drug release (%). Run 2 was found to be the optimized batch which was further evaluated on post compression parameters and the results were found to be within the specified limit. Detail comparative in vitro dissolution studies were performed for the optimized batch and the marketed preparation according to which the optimized batch showed satisfactory result. Accelerated stability studies were performed for the drug for a period of 3 months. In conclusion the tablet formulated and evaluated from the phytoconstituent showed satisfactory results.

Keywords: Alpha tocopherol, Phytoconstituent, solid dispersion method, Bioavailability, Solubility, nanocarrier, tablet.

https://doi.org/10.33887/rjpbcs/2023.14.4.2

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Since it made it possible to create nanoparticles with standardized compositions, shapes, and sizes, nanotechnology has become increasingly significant and valuable in the fields of science and drug delivery. Nanoparticles are solid colloidal particles with a size range of 1 to 1000 nm and a high molecular composition [1,2]. The active component is loaded or encapsulated within the nanoparticles [2]. The creation and assessment of a nanocarrier for a phytoconstituent are the topics of the talk. The chemical substances that are active and exist naturally in plants are called phytoconstituents. The 16 different categories of phytoconstituents include alkaloids, terpenoids, glycosides, tannins, vitamins, and carbohydrates etc. Numerous medications and phytoconstituents have limited water solubility, which results in reduced bioavailability; hence, the use of nanotechnology is the recommended solution to this problem [1].

Mesoporous Silica Nanoparticles

Mesoporous silica nanoparticles have changed the controlled drug delivery method. The greater pore volume, surface area, and other characteristics of their well-organized interior mesopores make them the ideal platform for developing nanosystem [2, 3]. Due to their perfect and ideal characteristics, mesoporous silica nanoparticles are referred to as the ideal nanocarriers to transport and preserve the drugs [4, 5].

Significance of incorporating phytoconstituent in to mesoporous silica nanocarrier [4, 5].

- To increase phytoconstituent solubility
- To increase the bioavailability
- To inhibit the component from chemical degradation
- To stabilize the drug.

Alpha tocopherol

Vitamin E, also known as alpha tocopherol, is a crucial part of the body's defense against free radicals. It is a fat-soluble vitamin that is further broken down into eight compounds: four tocopherols (α, β, γ, and δ) and four tocotrienols (α, β, γ, and δ), the latter of which has been determined to be the most active [6, 7]. Vitamin E's antioxidant function, which shields cells from reactive oxygen species and delays or prevents the onset of inflammatory and degenerative illnesses, is the most significant activity of Vitamin E. Studies revealed that those who ate more vitamin E-rich foods or who voluntarily opted to take a vitamin E dietary supplement had a lower incidence of dementia, cancer, and other diseases; however, placebo-controlled clinical trials were not always able to confirm these findings. Because tocopherols, both natural and synthetic, are prone to oxidation, they are esterified to produce tocopheryl acetate as a stabilising agent in dietary supplements [6-13]. Although vitamin E is necessary for health, the body can store some of it, so it is not necessary to ingest it every day. Typically, a food item high in fat is consumed together with this vitamin. The tolerated upper consumption threshold for vitamin E has been established based on age. There are several foods that contain vitamin E, including egg yolks, vegetable oil, almonds, cheese, soy beans, wheat germ, avocados, olives, and green leafy vegetables. Gamma-tocopherol, which is found in soybean, canola, corn, and other vegetable oils and food products, makes up the majority of vitamin E in American diets. Phytoconstituents, often known as phytochemicals, are substances made by plants that have been shown to exhibit antioxidant properties both in vitro and in human trials. Indoles, tocopherols, polyphenols, and other phytoconstituents are a few examples [14-18]. In tablet dosage form, the mixture of phytoconstituent and nanocarrier is examined further.

MATERIALS AND METHODS

The phytoconstituent alpha tocopherol was obtained from Sigma Aldrich. Syloid 244FP and Eudragit RL 100 were obtained from Grace Davison and Evonik industries. All the solvents and excipients used were of analytical grade.

Method Of Formulating The Phytoconstituent In To A Nanocarrier

The phytoconstituent was formulated in to a nanocarrier by solid dispersion method [5]. Silicon dioxide was used as a carrier which was mixed with the alpha tocopherol and was kept in an orbital incubator shaker for around 48 hrs in an optimum condition.

Preformulation Studies

Preformulation studies are one of the stages of research and development that describe the physical and chemical properties of a drug molecule and excipients in order to generate a stable, reliable, and safe dosage form.

Identification of phytoconstituent (α tocopherol) and characterization

Organoleptic properties

Alpha tocopherol was observed for it colour, odour and appearance by visual observation.

Study of α tocopherol

Specific quantity of alpha tocopherol was weighed and dissolved in different solvents such as water, chloroform, ethanol, methanol, acetone, ether and in fixed oil (oleic acid). After sonicating the solution for 30min it was kept aside for 24hrs and analysed by using UV-visible spectrophotometer [19, 20].

Pharmacognostic test for identification of phytoconstituent

About 5mg of alpha tocopherol was dissolved in 10ml of absolute ethanol to which 2-3ml of nitric acid was added and mixed simultaneously. The mixture was heated for 15 min at about 75^0C.

UV-Visible spectroscopy

Calibration curve for alpha tocopherol was performed in various solvents such as methanol, acetone, ethanol, mixture of acetone+ methanol to obtain the equation and R^2 value [19].

Preparation of stock solution

Stock solution was prepared for each solvent of concentration 100 and 1000µg/ml to find out fixed wavelength where the maximum peak is obtained [19].

Procedure for calibration curve of alpha tocopherol

After getting fixed wavelength different dilutions (that is 25, 50,100…..) were prepared from the stock in to a 10ml volumetric flasks. The final volume was made by the solvent used and absorbance was measured at a specific wavelength by using Shimadzu UV-1800 UV-visible spectrophotometer with quartz cells of 10mm path length [19].

Melting point

Melting point was carried out by using melting point apparatus.

Validation of UV-spectrometric method for alpha tocopherol

Validation of the phytoconstituent was done to check the liability, to assure that the product is of the quality and to prevent further risk [20, 21]. Alpha tocopherol was validated for

Linearity

According to ICH Q2B guidelines for the validation of analytical methods, the method was validated. It evaluates the concentration range for which the method can operate consistently [20, 21].

Precision

It defines the degree of repeatability of an analytical method under normal experimental conditions. The procedure was carried out in triplicates and its mean was taken. The precision was determined by intra-day (repeatability) and inter-day (intermediate precision) [21].

Robustness

It is the capacity of a method to remain unaffected by small changes in method parameters. For eg: Measurement of absorbance at different wavelength.

Ruggedness

It is an analytical method obtained by analyzing the same sample at different conditions such as different laboratories, different instruments, and different analyst.

Purity of alpha tocopherol

Refractive index

Refractive index of alpha-tocopherol was carried out by using refractometer

Experimental Work

Formulation and development of nanoparticles

Formulating the phytoconstituent in to a nanocarrier

- Different concentration ratio of carrier: phytoconstituent such as 1:1, 2:1 were prepared by solid dispersion method
- The carrier was mixed with the alpha tocopherol and was kept in to orbital incubator shaker for around 48 hrs in an optimum condition
- After incorporating the constituent in to a nanocarrier further studies were carried out.

Comparative study between two carriers

The phytoconstituent that is alpha tocopherol was incorporated in two different carriers such as Syloid 244FP and lactose in the ratio 1:1, 1:2 and dissolution studies were performed in two different solvents such as 0.1 N HCl and Phosphate buffer (PH 6.8). The dissolution medium was selected from the observed result.

Drug entrapped in the nanoparticles

After formulating the nanoparticles the entrapment efficiency was checked by evaluating the nanoparticles in three different solvents water, 0.1 N HCl and Phosphate buffer (PH 6.8). About 100mg of the nanoparticles were mixed with each solvent (Water, 0.1N HCl, phosphate buffer) and was filtered by using whatman filter paper. The residues that were obtained after filtration were taken around 10mg and were mixed with 10ml of methanol and again were filtered. The filtrate obtained was analysed at 292nm with the help of UV spectrophotometer and by applying formula the drug entrapped in the nanocarrier was found out.

Formation and optimization of alpha tocopherol tablets

The optimization of tablet was performed by 2^2 factorial designs [22]. A 400 mg tablet was prepared by direct compression method by using 12mm punch. The ingredients used in formulation were composite that is the mixture of carrier and phytoconstituent, Starch, Microcrystalline cellulose, Lactose and Eudragit RL100 as polymer.

Factorial design

2^2 factorial design

Independent variables

X_1- Different concentration of carrier (100-200mg), X_2-Different concentration of polymer (50-100mg)

Dependent variables

Y_1-Disintegration time (sec),
Y_2-Friability (%), Y_3-Drug release (%)

Evaluation of batches

By applying 2^2 factorial design about 4 experimental runs were obtained and disintegration time, friability, drug release were taken as response variable [23-26]. (Table no 1) provides the 4 experimental runs for optimization of tablet formulation.

Disintegration time

- 6 tablets from each run were evaluated for disintegration time and the result was noted down.
- Temperature of the bath was maintained at 37± 2^0C.

Tablet friability

- About 10 tablets were used for the evaluation of friability [24, 25].
- The tablets are weighed first and then put in to the friability tester and the drum is rotated for 100 times and after that the tablets are weighed again after dedusting.
- The formula for tablet friability is:

Weight difference (W_1) = Initial weight(X_1)- Final weight(X_2)
% loss of weight= W_1/X_1 *100

In vitro drug release

- Dissolution medium: 900 ml of phosphate buffer(6.8PH)
- Temperature: 37±0.5^{o}C
- Speed: 72 rpm
- Dissolution apparatus: Type 2(Paddle apparatus) USP

Selection and detail evaluation of optimized batch physical mixture

From the four runs the most optimized batch was selected and the composite mixture of the optimized batch was further evaluated in to [24-26].

Angle of repose: To create a cone, the substance is poured via a funnel. To lessen the effect of falling particles, the funnel tip should be kept near to the expanding cone and gently lifted as the pile rises. When the pile reaches a set height or the base a predetermined width, stop pouring the material.

Angle of repose= $\tan^{-1}$ h/r

Bulk density: The mass of many particles divided by the total volume they occupy is how bulk density is calculated. Particle volume, inter-particle void volume, and internal pore volume are all included in the overall volume.

Bulk density= Weight of powder/ bulk volume

Tapped density: The mass-to-volume ratio of a powder after it has been tapped for a specific amount of time is known as the powder's "tapped density."

Tapped density= weight of powder/Tapped volume

Carr's compressibility: It serves as an indicator for a powder's ability to be compressed. The bulk density and tapped density in a free-flowing powder would be close in value, resulting in a low Carr index. On the other hand, the bulk and tapped densities would be greater in a poorly flowing powder where there are more interparticle interactions, leading to a bigger Carr index.

Carr's index= Tapped density- Bulk density/ Tapped density *100

Hausner's ratio: It is correlated to the flowability of a powder or granular material. Poor flowability is deemed to be indicated by a Hausner's ratio of 1.25 to 1.4.

Hausner's ratio= tapped density/ bulk density

Detail evaluation of optimized batch tablet

Further detail evaluation was performed for the optimized batch of tablet such as [23- 28].

Hardness: Tablet hardness is sometimes referred to as the tablet crushing strength and is normally stated as the force required to crush a tablet when it is put on its edge. Hardness is typically a good indicator of a tablet's acceptability when it comes to mechanical stability during packaging and shipment. Using a tablet hardness tester (Monsanto) the crushing strength was assessed.

Thickness and diameter: A vernier caliper was used to measure the tablet's thickness and diameter. Depending on the size of the tablet, the thickness should be kept within a 5% range of a specified value.

Average weight: Twenty tablets were weighed individually using an analytical balance and the average weight were then calculated

Wetting time: A 6.5 cm diameter, folded-in-half piece of filter paper was placed on a water-filled petri dish. The test tablet was positioned in the centre of the filter paper that had been saturated with the solution until the tablet's contents were dispersed equally. The time needed for the water to diffuse from the wet filter paper was calculated using a timer.

Water absorption ratio: Water absorption ratio= 100(weight of tablet after water absorption-weight of tablet before water absorption) / weight of tablet before water absorption.

Weight variation: Twenty tablets were individually weighted using the analytical balance and average weight was calculated. The following is the equation for calculating percentage weight variation:

Weight variation= Initial weight-average weight/average weight *100

FTIR studies

Fourier transform Infrared Spectroscopy, which is also known as FTIR analysis is an analytical technique used to identify organic, polymeric material. The method uses infrared light to scan the samples and observe the chemical properties. FTIR spectra for carrier (Syloid 244FP), Composite of carrier: alpha tocopherol and optimized batch tablet were obtained by scanning the sample by using KBr

[29, 30]. About 1mg of the samples were triturated with 4mg of dry KBr and then pressed in to disks. The FTIR spectrum was recorded using Jasco 4100(TOKYO, JAPAN) with IR resolution software. The scanning range was 4000-650cm^{-1}.

XRD (X-RAY Diffraction) analysis

This study is used to study the crystalline phase which is present in material and predicts the chemical composition information. It is one of the non-destructive techniques for characterization of crystalline material [29, 30]. The study was done on the composite mixture (drug and syloid carrier) and on the tablet formulation.

Particle size

Particle size is performed to see whether the particles are of desired size and fall in to range. The particle size for the alpha tocopherol and the composite of carrier: drug was carried out in water, methanol, and water+methanol solvent. Using a particle size analyzer, the z-average particle size and particle size distribution of nanoparticles were examined.

Comparative study of formulated tablet with the marketed formulation

Dissolution testing measures the extent and rate of solution formation from a dosage form. Dissolution studies were carried out for the formulated tablet and the marketed formulation as the comparative study and the results were compared [31-33]. Vitamin E capsules USP 400mg (Evion) was used as the marketed formulation.

Stability studies

Stability testing was carried out to provide evidence of how the quality of the manufactured tablets may change with time under the influence of environmental factors such as temperature, humidity and storage. It was important and necessary for observing drug's degradation in the process of time. Accelerated stability studies were carried out at temperature 25±2°C/60±5% relative humidity for 3 months [34]. In stability studies, compressed optimized silica alpha tocopherol composite tablets were evaluated for average weight, diameter, thickness, hardness, friability.

RESULTS AND DISCUSSION

Preformulation studies

Identification of drug

Organoleptic properties, solubility and melting point of alpha tocopherol

The organoleptic properties, solubility and melting point are summarized in (Table no2).

Pharmacognostic test for identification of phytoconstituent

The end result for the following pharmacognostic test was appearance of bright red colour which identified the phytoconstituent as α tocopherol.

UV- visible spectrophotometry

Calibration curve for alpha tocopherol was performed in acetone, ethanol, methanol and in mixture of acetone+ methanol. The best results were obtained in methanol as compare to other solvent. According to Beers Lambert law, the absorption maximum was observed at 292nm for alpha tocopherol. Absorbance data and calibration curve of alpha tocopherol in methanol is given in following (Table no 3 and Figure no 1).

Validation of UV-spectrometric method for alpha tocopherol

Linearity: Concentrations ranging from 20 to 300µg/ml were prepared of Alpha tocopherol in methanol. Each sample was analyzed in triplicate; calibration curve was constructed by plotting the absorbance against concentration using linear regression analysis. The R2 value and regression equation was found to be 0.996 and Y= 0.0036x-0.0227 respectively.

Precision: Here the assay was repeated three times on a same day to determine the repeatability(intra-day precision) and for determining intermediate precision the assay was performed on three consecutive days(Inter-day precision).The Intra-day precision study showed a RSD of 0.8124% for 200µg/ml and 1.7698 % for 250 µg/ml concentrations.. Inter-day precision study showed a RSD of 1.45% for 200µg/ml and 0.58 % for 250 µg/ml concentrations. Thus, it can be concluded that the study showed a good intraday and Interday precision indicating high precision of the methods.

Robustness: The robustness was assessed at two different wavelengths, 290 and 292 nm, respectively, and the impact of a change in wavelength was investigated by calculating %RSD, which revealed insignificant variation on the outcomes, as shown in (Table no 4).

Ruggedness: The degree of reproducibility of test results was investigated by calculating % RSD. Here the sample was analyzed by two different U.V instruments: Instrument A (Jasco-V 630) and Instrument B (Shimadzu AUX 220) and the results were obtained as shown in (Table no 5).

Purity of alpha tocopherol

Refractive index

Refractive index of alpha-tocopherol was found to be 1.505; which was found to be in range 1.503-1.508 indicating the purity of alpha-tocopherol.

Result & Discussion For Formulation And Evaluation Of Silica- α-TP Composite Tablets

Comparative study between two carriers

Physical mixture of phytoconstituent was made in two carriers that are lactose and syloid 244FP in the ratio 1:1. Dissolution studies were carried out for both carriers in 0.1N HCl and Phosphate buffer (PH 6.8) and the results were obtained as shown in (Table no 6 and Table no 7).

By comparative studies it was found out that the use of lactose carrier to incorporate the drug was found to be not suitable as compare to use of syloid 244FP as nanocarrier. The lactose and drug mixture showed irregular and non-consistent result in 0.1N HCl medium whereas in phosphate buffer it showed relatively nice result with some irregularity.

The syloid and drug mixture showed consistent result in phosphate buffer and relatively better result as compare to 0.1N HCl medium. About 94% of drug was released in 20 min in phosphate buffer medium. Whereas in case of HCl the drug release from the carrier was found to be 23.44% within 2 hrs.

Drug entrapped in the syloid nanocarrier

From (Table no 8) the drug entrapped in the nanocarrier was found to be in the order of phosphate buffer> 0.1 N HCl> water.

Evaluation of batches

The four runs obtained by applying 2^2 factorial design were further evaluated for their disintegration time, friability and drug release. Run 2 results were found to be relatively good as compare to other runs as shown in (Table no 9). By putting these obtained value for all runs in the stat ease optimization software the run 2 was found to be the optimized batch.

(Table no 10) provides the flow properties and post compression parameters of optimized formulation (Run 2).

In vitro drug release kinetics for optimized batch of tablet (Run 2)

The potential of nanoparticles to modulate medication release is shown by their in vitro release kinetics, which is an important metric to take into account when evaluating the products' safety, effectiveness, and quality. (Table no 11 and Figure no.2) shows the drug release kinetics.

FTIR (Fourier Transfer Infrared Spectrophotometer)

(Figure no 3, 4 and 5 and Table no 12, 13 and 14) provides with the FTIR spectra and its interpretation for the carrier (Syloid 244FP), Nanoparticle of Alpha tocopherol encapsulated in syloid nanocarrier and optimized tablet. All three composition generated FTIR spectra with clear bands. O-Si-O bending main functional group of pure carrier syloid 244FP was found out to be present in nanoparticles and even in optimized tablet interpretation which indicates the presence and proper binding of drug with the carrier.

X- Ray Diffraction

The synthetic vitamin E nanoparticles' X-ray diffraction results revealed that the substance is amorphous in nature. The XRD peaks are located at 2θ= 42.7, 46.3 and 64.9(Figure no.6)

Particle size distribution

Particle size of the phytoconstituent (alpha tocopherol), composite mixture of optimized batch and syloid was performed in solvents such as water, methanol and mixture of water+ methanol. The desirable results were found in mixture of water+ methanol as compare to other solvents (Figure no.7 and Figure no.8). Alpha tocopherol showed mean particle size of 545nm.

Comparative study of formulated tablet with the marketed formulation

Dissolution studies were carried out for the optimized batch of tablets formulated of alpha-tocopherol in phosphate medium (PH6.8). The results were compared with the dissolution studies performed for the marketed formulation of vitamin E capsule in phosphate buffer itself (Table no.15 and Figure no.9). Evion 400 which is a capsule of Vitamin E USP400mg was used for comparative study. From the result it was seen that after 40 minutes the marketed formulation showed about 52.42% of drug release whereas the formulated optimized batch showed 86.02% of drug release which was found to be a better.

Stability studies

Testing for stability under expedited circumstances the optimized vitamin E tablets were demonstrated to be stable over a three-month period at 25±2°C/60±5% relative humidity by the lack of substantial alterations in their physical characteristics and in the following parameters (Table no.16).

Table 1: Trial batches for optimization of tablet formulation

Ingredients(mg)	Run 1	Run 2	Run 3	Run 4
Composite (carrier+ drug)	200+100	100+100	200+100	100+100
MCC	25	33.3	-	100
Starch	25	33.3	-	50
Lactose	-	33.3	-	-
Eudragit RL 100	50	100	100	50

ISSN: 0975-8585

Table 2: Organoleptic properties, solubility and melting point of alpha tocopherol

Preformulation parameters	Observation
Colour	Brownish colour
Odour	Odourless
Appearance	Semisolid
Solubility	Insoluble in water, soluble in ethanol, methanol, miscible with ether, acetone and it is soluble in fixed oil
Melting point	3^0C

Table 3: Absorbance value for development of calibration curve in methanol

Sr.No.	Concentration(µg/ml)	Absorbance
1.	20	0.03256±0.00047
2.	25	0.05229±0.00022
3.	50	0.16552±0.00043
4.	100	0.33950±0.00040
5.	150	0.50896±0.00013
6.	200	0.71587±0.00011
7.	250	0.89287±0.00011
8.	300	1.00029±0.00013

Table 4: Robustness of alpha tocopherol in methanol

Wavelength (nm)	Average±S.D.	% RSD
290	0.749±0.06599	8.81
292	0.759±0.06729	8.86

Table 5: Ruggedness of alpha tocopherol due to instrument A and Instrument B

Concentration (µg/ml)	%RSD	
	Instrument A: (Jasco-V 630)	Instrument B: (Shimadzu AUX 220)
200	8.84	0.82
250	0.53	0.51

Table 6: Dissolution study of drug and lactose carrier mixture in phosphate buffer and 0.1 N HCl

Time(min)	% drug release	
	Phosphate buffer(PH 6.8)	0.1N HCl
10	34.64	57.69
15	80.194	-
20	84.36	-

ISSN: 0975-8585

Table 7: Dissolution study of drug and syloid carrier mixture in phosphate buffer and 0.1 N HCl

Time(min)	% drug release	
	Phosphate buffer (PH 6.8)	0.1N HCl
2	42.31	-
5	45.77	4.2
15	49.27	7.9
20	94	-
30	-	8.91
45	-	9.1
60	-	11.94
90	-	22.05
120	-	23.44

Table 8: The percentage of drug entrapped in the nanocarrier

Sr.No.	Solvents	Drug entrapped (%)
1.	Water	79.73
2.	Phosphate buffer	96.48
3.	0.1N HCl	92.43

Table 9: Observed responses from runs in 2^2 factorial design

Parameters	Run 1	Run 2	Run 3	Run 4
Average of disintegration time(sec)	205.6±10.577	191.16±1.037	3937.83±160.1	35.16±0.752
Average of friability (%)	12.05±0.0866	1.53±0.5456	1.31±0.0655	7.49±0.0964
Drug release (%)	92.97±2.060	91.31±0.292	13.81±0.185	72.14±2.521

Table 10: Flow properties and Post compression parameters of optimized formulation (Run 2)

Flow properties/ Post compression parameters	Optimized formulation(Run 2)
Flow properties Angle of repose	28.55±2.0754
Bulk density	0.0689±0.0068
Tapped density	0.0769±0.0049
Carr's index (%)	10.20±0.3464
Hausner's ratio	1.11±0.0360
Post compression parameters Thickness(mm)	3.76±0.052
Diameter(mm)	11.89±0.0635
Hardness(Kg/cm^2)	2.83±0.26
Average weight(mg)	393±3
Weight variation (%)	1.71±0.0264
Wetting time(sec)	403±3
Water absorption ratio (%)	68.43±5.93
Disintegration time(sec)	190±1
Friability (%)	0.93±0.03

ISSN: 0975-8585

Table 11: Drug release profile for optimized batch (Run 2)

Time(min)	% drug release
10	12.97
15	24.91
20	32.97
25	43.25
30	52.97
35	64.91
40	86.02

Table 12: Interpretation of IR of syloid 244FP carrier

Syloid 244 FP carrier	
Positions	**Functional group**
655.679	O-Si-O bending
1613.16	Si-O-Si stretching

Table 13: Interpretation of IR of Physical mixture of alpha tocopherol+ syloid

Physical mixture of alpha tocopherol+ syloid	
Positions	**Functional group**
670.142	O-Si-O bending
1104.05	C-O stretching
1639.2	C=C stretching
2933.2	C-H alkane
3340.1	Terminal O-H stretch

Table no. 14: Interpretation of IR of optimized batch of tablet

Optimized batch of tablet formulation (Run 2)	
Positions	**Functional group**
661.464	O-Si-O bending
1108.87	C-O stretch
1629.55	C-C stretching
2362.37	C-H alkane
3410.49	Terminal OH stretch

Table no.15: In vitro drug release of marketed formulation (Evion 400)

Time(min)	% drug release of marketed formulation	% drug release of optimized batch (Run 2)
10	9.33	12.97
15	16.31	24.91
20	22.42	32.97
25	29.08	43.25
30	35.47	52.97
35	42.14	64.91
40	52.42	86.02
45	69.92	-

ISSN: 0975-8585

Table 16: Summary of stability studies for optimized batch (Run 2)

	Parameters				
Time (Month)	Average weight	Diameter	Thickness	Hardness	Friability
0 month	393±3	11.89±0.0635	3.76±0.052	2.83±0.26	0.93±0.03
1 month	393±2	11.89±0.01	3.76±0.06	2.83±0.42	0.92±0.02
2 month	394±1	11.88±0	3.74±0.02	2.82±0.01	0.91±0
3 month	395±1	11.88±0.02	3.74±0.04	2.81±0.01	0.88±0.01

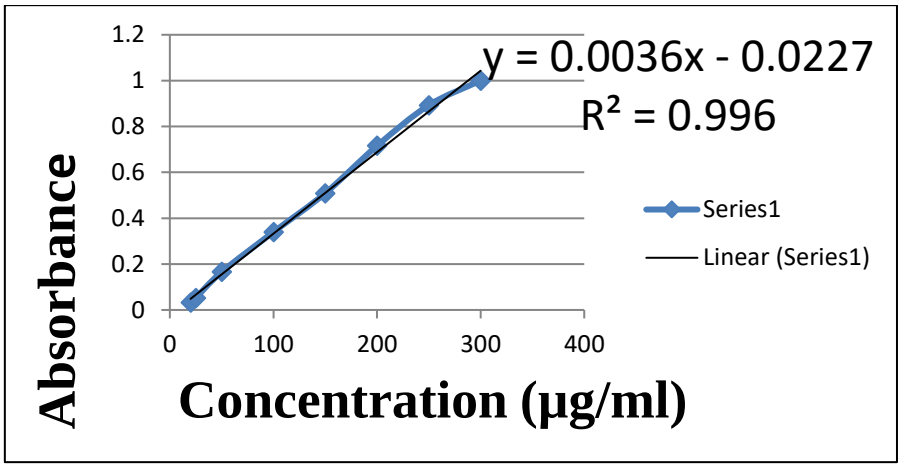

Figure 1: Calibration curve of alpha tocopherol in methanol

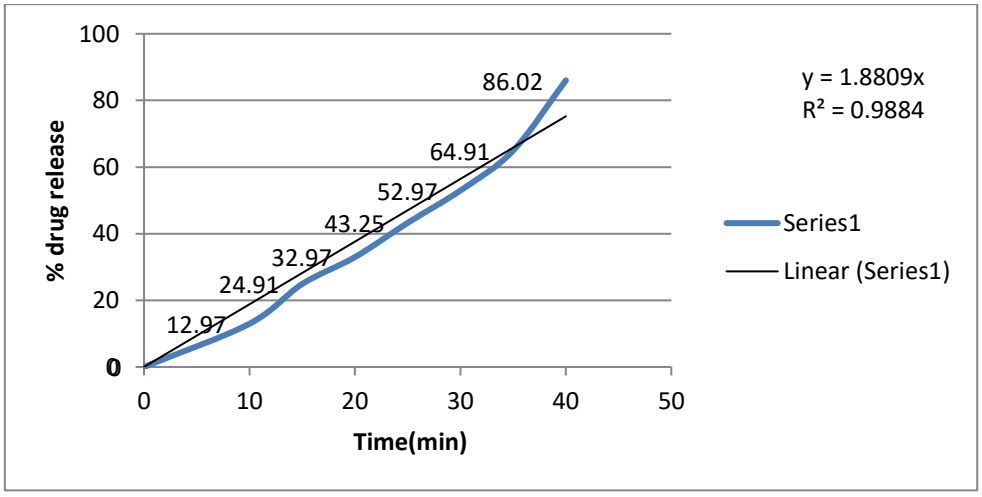

Figure 2: In Vitro drug release profile for optimized batch of tablet

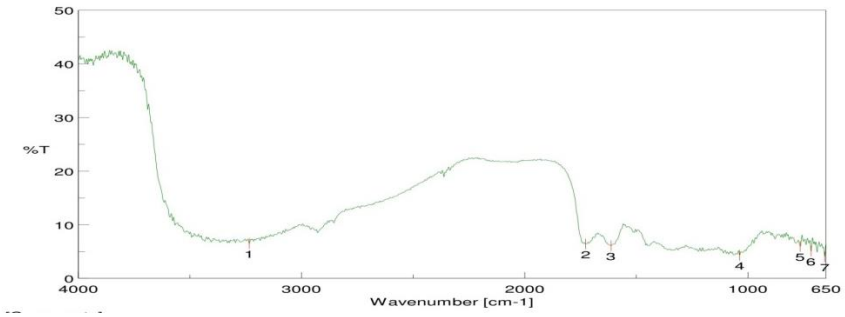

Figure 3: FTIR spectra of syloid 244FP carrier

ISSN: 0975-8585

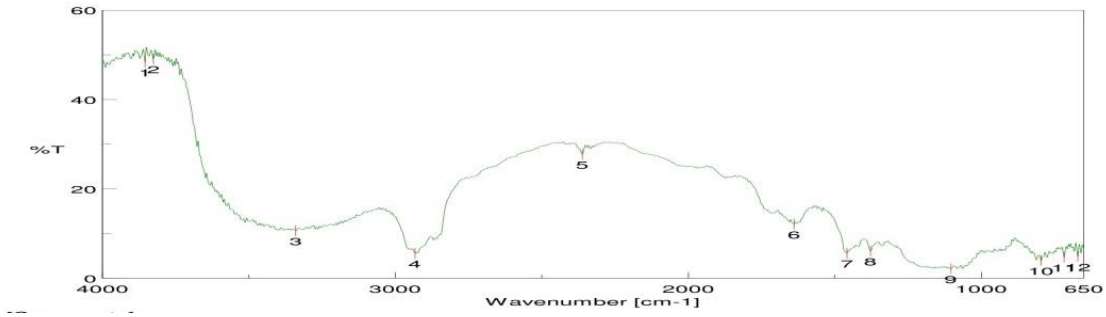

Figure 4: FTIR spectra of physical mixture of alpha tocopherol+ syloid

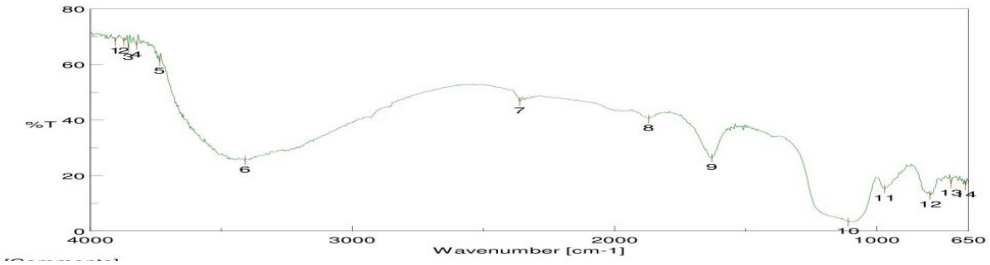

Figure 5: FTIR spectra of optimized batch of tablet (Run 2)

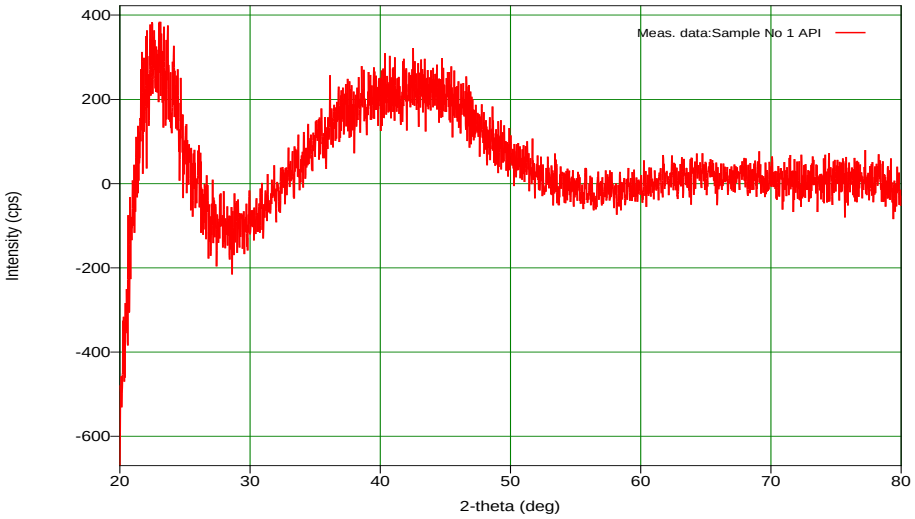

Figure 6: XRD of the composite mixture

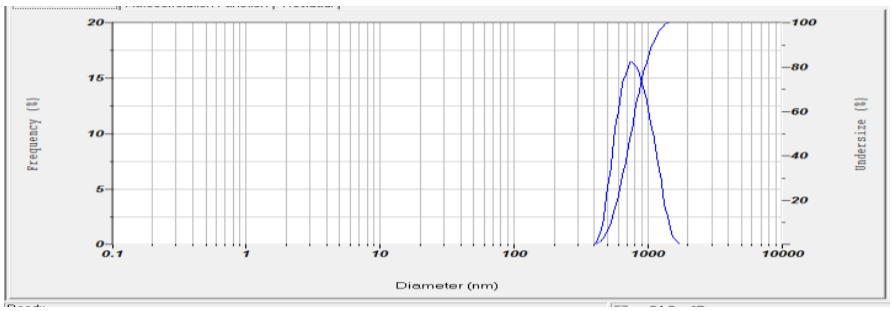

Figure 7: Particle size distribution of vitamin E

ISSN: 0975-8585

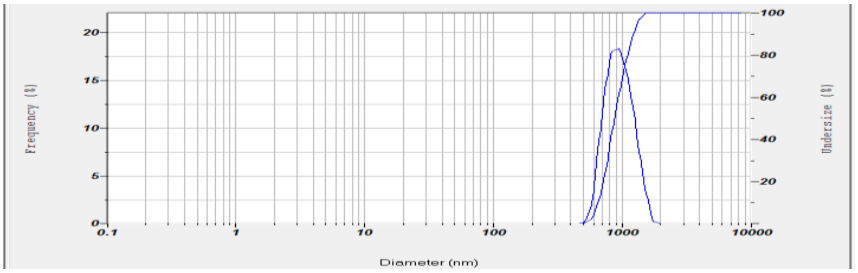

Figure 8: Particle size distribution of optimized batch of mixture of Vitamin E+ syloid

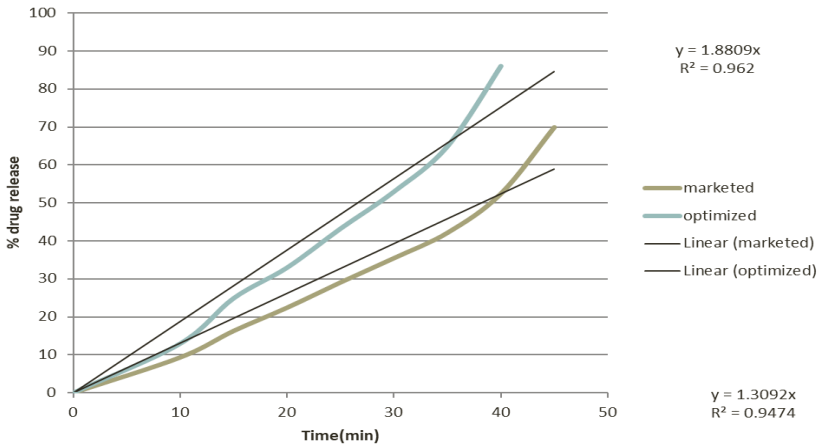

Figure 9: Comparative In vitro drug release profile of marketed formulation and Formulated optimized batch

CONCLUSION

In the present work of formulation and evaluation of silica alpha tocopherol composite using solid dispersion technique and converting it in to a tablet dosage form were performed successfully. The aim behind formulating the phytoconstituent in to a nanocarrier was to overcome the limitations which may be due to poor solubility and dissolution. Detailed Optimization studies were performed by using 2^2 factorial design and evaluation was carried out for the optimized batch of tablet. FTIR and particle size were also performed for the nanocarrier, physical mixture and optimized batch of tablet. The nanocomposite formed was observed for their drug content, entrapment efficiency. The results were encouraging for the optimized alpha tocopherol composite tablet. The tablet formulated for the alpha tocopherol was found to be better in comparison to the available marketed formulation for the drug in respect to in vitro dissolution studies and stability of formulation.

ACKNOWLEDGEMENT

Authors are thankful to the department of pharmaceutics, PES, Modern college of pharmacy, Nigdi, Pune for providing all laboratory facilities to carry out this research.

REFERENCES

[1] Melzig S, Niedbalka D, Schilde C, wade AK. Spray drying of amorphous ibuprofen nanoparticles for the production of granules with enhanced drug release. Colloids and Surfaces A 2018; 536:133-141.

[2] Regí MV, Montserrat C, Barba II and Manzano M. Mesoporous Silica Nanoparticles for Drug Delivery: Current Insights. Molecules 2018; 23(1): 47.

[3] Baeza A., Colilla M., Vallet-Regí M. Advances in mesoporous silica nanoparticles for targeted stimuli-responsive drug delivery. *Expert Opin. Drug Deliv* 2015;12:319–337.

[4] Bharti C, Nagaich U, Pal AK, Gulati N. Mesoporous silica nanoparticles in target drug delivery system: A review. Int J Pharm Investig (2015); 5(3):124-33.

[5] Chaudhari SP and Gupte A. Mesoporous Silica as a Carrier for Amorphous Solid Dispersion. British Journal of Pharmaceutical Research(2017); 16(6): 1-19.
[6] Rizvi S, Raza ST, Ahmed F, Ahmad A, Abbas S, Mahdi F. The role of vitamin e in human health and some diseases. *Sultan Qaboos University Medical Journal* 2014; 14(2): e157-e165.
[7] Etsuo N and Kouichi A. CHAPTER 1: Vitamin E: Structure, Properties and Functions. *Vitamin E: Chemistry and Nutritional Benefits* 2019; pp. 1-11.
[8] Traber MG, Atkinson J. Vitamin E, antioxidant and nothing more. Free Radic Biol Med. 2007; 43(1):4-15.
[9] Qureshi AA, Khan DA, Silswal N, Saleem S, Qureshi N. Evaluation of Pharmacokinetics, and Bioavailability of Higher Doses of Tocotrienols in Healthy Fed Humans. J Clin Exp Cardiolog 2016; 7(4): 434.
[10] Brigelius-Flohé R, Traber MG. Vitamin E: function and metabolism. FASEB J 1999; 13(10):1145-55.
[11] Schmölz L, Birringer M, Lorkowski S, Wallert M. Complexity of vitamin E metabolism. World J Biol Chem 2016; 7(1):14-43.
[12] Kim HJ, Giovannucci E, Rosner B, Willett WC, Cho E. Longitudinal and secular trends in dietary supplement use: Nurses' Health Study and Health Professionals Follow-Up Study, 1986-2006. J Acad Nutr Diet 2014;114 (3):436-443.
[13] https://go.drugbank.com/drugs/DB11251
[14] https://ods.od.nih.gov/factsheets/VitaminEHealthProfessiona/#h5
[15] Ohkatsu Y, Kajiyama T, Arai Y. Antioxidant activities of tocopherols. Polymer degradation and stability (2001); 72(2):303-311.
[16] Hategekimana J, Masamba KG, Ma J, Zhong F. Encapsulation of vitamin E: effect of physicochemical properties of wall material on retention and stability. Carbohydrate Polymer (2015); 124:172-9.
[17] https://pubchem.ncbi.nlm.nih.gov/compound/DL-alpha-Tocopherol
[18] Colombo ML. An update on vitamin E, tocopherol and tocotrienol-perspectives. Molecules (2010); 15(4):2103-13.
[19] Saeed AM, Al-Kadumi AS and Mohammed Ali NJ. Spectrophotometric determination of vitamin E formation of gold complex. European Journal of biomedical and pharmaceutical science (2017); 4(7): 82-87.
[20] Wahab SI, Mouzam MI, Tadwee I. Simplistic spectroscopic method for determination of α-Tocopherylacetate in bulk and formulated microemulsion. IJPRAS(2013); 2(3): 64-67.
[21] Gaur A , Rathore P. Simultaneous Estimation of Ambroxol Hydrochloride and Olopatadine in Formulated Tablet Dosage Form by UV Spectroscopic Method. International Journal of Pharmaceutical Quality Assurance 2016; 7(4): 62-65.
[22] Syed IA, Patro C , Alshanberi AM, Ansari SA. Statistical Designing and Characterization of Valsartan Oral Disintegrating Tablet. Advances in Pharmacology and Pharmacy (2021);9(3): 33-44.
[23] Jakaria M, Mousa A Y, Parvez M, Zaman R, Arifujjaman, Sayeed M A, Ali M H. In vitro Comparative Study of Different Brands of Dexamethasone Tablet Available in Bangladesh. International Journal of Pharmaceutical Quality Assurance 2016; 7(2): 24-28.
[24] Indian Pharmacopoeia 2010; published by The Indian Pharmacopoeia Commission Ghaziabad; Volume I: 559-560.
[25] Indian Pharmacopoeia 2010; published by The Indian Pharmacopoeia Commission Ghaziabad; Volume III: 1754-1755.
[26] Indian Pharmacopoeia 2010; published by The Indian Pharmacopoeia Commission Ghaziabad; Volume II: 1554.
[27] Mr. Yadav DB, Mr. Rana HA, Dr. Maheshwari M, Dr. Patani P. Post compression evaluation parameters of paracetamol tablets: a review. JETIR(2020); volume 7(2): 1243-127
[28] Sukase GP, Autade YP , Pawar VD and Kurhe AR. Pre and post compression parameters of tablet and manufacturing defects. World journal of pharmaceutical research; volume 8(2): 432-439
[29] Pavia DL, Lampman G and Kriz G. Introduction of spectroscopy. Saunders college division. (2001); 3rd edition.
[30] Silverstein RM, Webster FX. Spectrometric identification of organic compounds. Wiley India (2011); Sixth edition: 84-85.
[31] Saharan VA and Kukkar V. Dissolution enhancement of drugs Part I: Technologies and effect of carriers. International journal of Health research (2009); 2(2):107-124.

[32] Waters LJ, Hanrahan JP et al. Enhancing the dissolution of phenylbutazone using Syloid® based mesoporous silicas for oral equine applications. Journal of Pharmaceutical Analysis(2018); 8(3): 181-186.
[33] Sachan AK, kumar V, Kumar S,Kumari K and kumar J. Formulation and evaluation of α tocopherol acetate tablet by liquid solid technology. IJPSR (2019);10(1): 329-336.
[34] Tesfa Y, Kaleab A, Tsige GM. Accelerated stability studies of Glinus Iotoides tablets. Ethiopian Pharmaceutical Journal 2007; 25(1): 43-50