Journal of Advanced Pharmaceutical Sciences and Natural Products

FORMULATION, OPTIMIZATION AND EVALUATION OF EXTENDED RELEASE TABLET OF CYANOCOBALAMIN BY USING POLYMER MATRIX SYSTEM

Shivani Sharma*, Anuradha Singh, Babita Kumar

Corresponding author: Shivani Sharma

Email: shivani22-mpharm@sanskar.org

ABSTRACT

Cyanocobalamin Extended Release tablet final formulation was pre-pared wet granulation method using Polymer System. The pre-compression para-meter values that were assessed & optimised showed good free-flowing properties and fell within the specified ranges. The post-compression characteristics, including hard-ness, friability, & wt. fluctuation, in vitro disintegration time, and drug content for preparation of tablets have been evaluated. The present investigation was under-taken to fabricate & evaluate a Release tablet of Cyano-cobalamin by wet granulation method. All the formulations were subjected to Accelerated stability program, under stress condition to study the effect of temperature and humidity as guidelines. It is evident that the most of the Extended Release tablets were unaffected in respect of colour stability after 3 months. No appreciable change in physical characteristics, size & shape, & drug content was observed even after the evaluation for 3months storage. No appreciable change in physical characteristic, weight variation, hardness, thickness, % friability, % drug content and in-vitro drug release amount was observed even after the evaluation for 3- months' storage. Oral administration of dosage form should lead to appropriate distribution & show activity of therapeutic moiety depending on the characteristic of dosage form and drug. Among these formulated Extended Release tablets of Cyanocobalamin, Formulation (F5) was found to be best because release of drug in 12 Hours was found to be NLT 90.0 %.

Keywords: Cyanocobalamin HCl, Sustained Release tablets, Extended Release Tablet

INTRODUCTION

Oral Drug Delivery System:

Oral conveyance medications by a wide margin the most reasonable medicine delivery process due to its ease of administration, patient consistency, plan flexibility, and other factors. Oral medication delivery systems, including oral medicine administration systems, make for a significant portion of the medication conveyance frameworks available on the market advanced over time from timely delivery to site-specific delivery. Every patient may have a continuing desire for best possible drug delivery system that addresses two basic characteristics of single-portion and less continuous dosing over the course of treatment. The measurements structure should deliver dynamic medication straightforwardly at site of activity. In order to avoid this, definitions of oral supported controlled discharge have been created trying to deliver the medication gradually into GIT and keep a viable medication fixation. [1]

Different sorts of medication conveyance frameworks for oral organization, for example, rate controlled convey frameworks, time-controlled conveyance frameworks & site-explicit conveyance framework have been widely evolved instances rate controlled & time-controlled conveyance framework, supported retention restricted travel season measurements structure assimilation the ingestion site on grounds that, from there on the delivered drug isn't retained.[2]

GASTRO-INTESTINAL TRACT(GIT):

GIT, often known as human gastrointestinal tract, is an organ system responsible for devouring & processing staples, engrossing supplements, & ousting waste. The parcel comprises of stomach & digestive organs, is parted into plots of upper & lower digestive tracts. Every graphic across mouth butt is incorporated into GI lot.

Then again, the stomach related framework is a more extensive term that involves different designs, including stomach related organs. The GI lot discharges chemicals to assist with directing stomach related procedure

Limitations of Conventional Oral Dosage Form:[3]

- Seesaw changes; unfortunate patient consistency;
- Likelihood of missing chunk.
- Various medication treatment improves the gamble of harmfulness generally treatment.

Approaches to Over-come these Limitations:[4]

- Creation of new, safer, & better medications with longer half-lives & a wealth of helpful data;
- The safe and effective use of medications that are already on the market by applying the ideas and methods of regulated and authorized drug delivery systems.

Extended Release Drug Delivery System:

Broadened discharge plan a significant program for new medication innovative work to meet a few neglected clinical requirements viz. gives increment bioavailability of medication item, decrease in the recurrence of organization to drag out span of compelling blood levels, Diminishes the variance of pinnacle box focus and aftereffects and potentially works on the particular appropriation of the medication. Expanded discharge drug conveyance framework accomplishes a sluggish arrival of the medication over a lengthy timeframe or the medication is retained over a more drawn out timeframe. How much medication is delivered at a controlled rate (support portion, DM) to keep up with the specific blood levels for want timeframe.[5]

Desired Criteria for Extended RDDS:[6]

- The medications must formed an ERDDS ought to meet following boundaries.
- It should be stable in GIT medium & be able to be taken orally.
- Ideally, a medicine with a half-life of 2-4 hours would be a good candidate to be included in emergency room dosage formulations, such as captopril or salbutamol sulfate.

The aim of the study was formulation, optimization, and assessment of Cyanocobalamin Extended-Release Tablet Using Polymer Matrix System

MATERIALS AND METHODS

Materials used:

The materials were either AR/LR grade were used as supplied by manufacturer.

Methods:

Identification of drug:

Organoleptic Characteristics:

The drug's color, taste, and odor were described and noted.

Determination of Melting Point:

The medication stored a digital melting point equipment after being poured into a fused capillary tube on one end.[7]

Determination of functional groups by FTIR:

KBr discs made utilising a KBr press & hydrostatic pressure of 6–8 tonnes. After then, FTIR spectra will be captured within the 400–4000cm scanning range **(IP 2010).**

Drug Excipients Compatibility study:

By dispersing drug & formulation mixture in KBr using a Fourier infrared, the infrared spectra of pure drug & formulation mixture were captured Spectrophotometer after pure drug, excipients, &KBr were combined in 1:3 ratio & formed into pellets. After establishing a base-line association using dried KBr, FTIR spectra of dry drug combination, formulation mixture, &KBr were captured.[8]

Solubility

The determination of Cyanocobalamin's solubility was done in CH3OH, H2O, CH3OH, & CCl4. 10-millilitres of each solvent were added gradually to surplus drug in a beaker, which was then sealed with aluminium seals. After shaking solution, it was left to equilibrate for a whole day. After being centrifuged for 5-minutes in ultra-centrifuge, solutions with extra medication were filtered using Whatsman filters. Using a UV-visible spectrophotometer, filtrate was examined.[9]

Determination of Partition Co-efficient:

The partition co-efficient of cyanocobalamin in H2O was computed using an equal amt. of n-octanol as oil phase & H2O as aqueous phase. In a separating funnel, these 2-phases were mixed in equal parts with required dosage of medication. The mixture was then shaken by hand until equilibrium was reached. The sepa-rating funnel was then set aside for 20 minutes. Following this, aqueous phase was filtered, 1ml of it was taken, diluted with H2O, & absorbance of cyanocobalamin in aqueous phase was measured using a UV spectrophotometer at 345nm.[10]

Analytical Method:

Determine the Wavelength (λ_{max}) in Different Media:

Determination the wavelength (λ_{max}) of Cynocobalamin in H_2O:

A dilution of 1mg/1ml (1000 ppm) stock solution may be made by dissolving 50mg of cyanocobalamin in 50ml of (H2O) & sonicating mixture for 15 minutes in a bath sonicator. We can make a 2-10-ppm solution from this stock solution. Cyanocobalamin HCl's wavelength will be determined by scanning the medication at its normal λmax.

Determination The wavelength (λ_{max}) of Cynocobalamin in Methanol:

Cyanocobalamin's made by dissolving 50mg drug 50 ml of CH3OH, letting it sit in a bath Sonicator for 15 minutes, & then creating a dilution of 1mg/1ml (1000 ppm) stock solution. We may get 2–10ppm of solution from this stock solution. Cynocobalamin HCl's wavelength will be determined by scanning the medication at its normal λmax.[11]

Determination of Flow Properties:[12,13]

Carr's index was determined by following formula:

Carr's Index= tapped density-bulk density/tapped density×100

Hausner's ratio was determined by the following formula:

Hausner's Ratio = Tapped density/bulk density

Bulk Density: (Subrahmanyam 2nd edition)

Loose BD = wt. of Powder/Vol. of Packing

TBD = wt. of powder/ tapped vol. of packing

Tapped Density:

The mixture's weight (M) was determined by measuring the minimal volume (Vt) that was contained within cylinder

TD = wt. of mixture/minimum vol. occupied

Angle of Repose:

The angle of repose was determined by formula

$\tan\Theta = h/r$

Where,

θ = Angle of repose.

h = Height.

r = Radius.

Uniformity of Drug Content (%Assay):

Twenty different formulations of tablets will be weighed separately & ground into powder. The drug content will be measured by measuring absorbance at 345nm following appropriate dilution using a UV/Visible Spectro-photometer after powder equal to the average wt. of tablets is weighed & drug is extracted in methanol.

Preparation of Extended Release Tablets of Cyanocobalamin:

Granules for Cyanocobalamin (1500mcg or 1.5mg) tablets firstly sifted HPMC K4M, HPMC K15M, Microcrystalline Cellulose & Di Calcium Phosphate (Anhydrous) through #40 & collected in poly bag. Then sifted Cyanocobalamin through #100 triturate with the fines of above sifted materials. Geometrically mixed sifted Cyanocobalamin with sifted materials to make bulk. Dry mixing is then done for 10 minutes in double poly bag. Then granulate the dry mixed blend thoroughly with (isopropyl alcoholic polyvinyl pyrrolidone K-90) initially air dry for 10 minutes in tray dryer. Then followed by heating at 45°C for 30 minutes #24 and oversized retained quantity manually crushed and pass through #24. Then sifted lubricants as

HPMC K-15M, HPMC Methocel K4M, Colloidal Silicon Dioxide (Aerosil 200) & Talc through #40 & collected in separate poly bag. Then sifted Magnesium Stearate through #60 & collated separately. Lubrication is then done by mixing dried sifted granules& lubricants in blender for 15 minutes then added sifted magnesium Stearate & further blending is done for 03 minutes & final in-process parameters checked [58].

Table 1: Formulation

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6
Cyanocobalamin	**1.5**	**1.5**	**1.5**	**1.5**	**1.5**	**1.5**
HPMC K-15 M	10	15	25	40	60	70
HPMC Methocel K4M	50	55	50	25	35	40
Microcrystalline Cellulose	90	70	66	82	65	65
Di Calcium Phosphate (Anhydrous)	81	91	87	73	66.5	55
Polyvinyl Pyrrolidone (K90)	3	3	4.5	4.5	6.0	5.0
Isopropyl Alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Talc	1.5	1.5	2.0	2.0	2.0	2.0
HPMC K-15 M	20	30	20	25	22	22.5
HPMC Methocel K4M	40	30	40	45	37	35
Colloidal Silicon Dioxide (Aerosil 200)	1.5	1.5	2.0	2.0	2.0	2.0
Magnesium Stearate	1.5	1.5	2.0	2.0	2.0	2.0

Evaluation Parameters of Extended Release Tablets of Cyanocobalamin:

Wt. Variation Test:

To make sure a pill has right amount of medication, its weight will be measured. To perform the USP weight variation test, 20 tablets will be weighed separately, average weight will be determined, & individual wts. will be compared to average.

Hardness:

The tablet's hardness will be assessed using the Monsanto hardness tester. The tablet will be supported by both a stationary and movable jaw. After setting scale to zero, weight was progressively increased until tablet broke. The tablet's hardness is determined by the load value at that location. Kg/cm2 was used to express hardness.

Friability:

Friabilator (Electro Lab India) will test strength of tablet. After 100 rotations (4 minutes), pre-weighed pills will be removed & subtracted. By rewriting pills, the % weight reduction will be determined. The following formula will then be used to determine % of friability. [14]

$$F = w1\text{-}w2/w1\times100$$

Thickness & diameter:

The tablet's thickness and diameter will be measured with vernier callipers. It will be measured in millimeters.

Loss on Drying:

Determine on 1g by drying in LOD Apparatus at 60°C Temperature.

Determination of % Yield:

The prepared formulations' % yield value computed as a percentage of total quantities of medication & polymers used in the preparation.[15]

% yield = theoretical yield/practical yield×100

In-Vitro Drug Release Profile:

In vitro dissolution tests were performed using a USP type-I dissolution apparatus, operated at a rotation speed of 50rpm. The dissolution was conducted over 8-hours, initially using 900ml of 0.1N HCl (pH 1.2) as dissolution medium at a temp. of 37±0.5°C for first two hours, followed by 900ml of a pH 7.4 phosphate buffer solution for remaining duration. At specified intervals, a 5ml aliquot was withdrawn, & abs. was measured using a UV spectrophotometer set to 274nm.

Release Kinetics:

Dissolution data was fitted to Zero order, 1st order, Higuchi, & Korsmeyer-Peppas in order to identify kinetic modeling of drug release. The model was employed to ascertain which model was best. The release kinetics of cyanocobalamin (SR) from mouth were explained by fitting data from in vitro release into several equations.

Stability Study:

Stability tests were performed under accelerated conditions (40°±2° C at 75% RH±5% RH) for optimized F9. Matrix tablets were carefully wrapped in aluminum foil & stored at 40°±2° C & 75% RH±5% RH for 3-months in order to increase temperature. Samples were removed at end of first, second, & third months. Samples were tested for hard-ness, drug content, & in-vitro drug release.

RESULTS & DISCUSSION

IDENTIFICATION STUDY:

Organoleptic Characteristics:

Table 2: The Organoleptic Properties of Cyanocobalamin as well as following,

S.NO.	Organo-leptic Pro-perties	Result
1.	Colour	Dark Red Crystal or crystalline powder
2.	Door	Crystalline powder
3.	Odor	Odourless
4.	Taste	Tasteless

Determination of Melting Point:

Table 3: Result of Melting Point Cyanocobalamin.

Method Employed	M.P	Observed M.p
	Cyanocobalamin	Cyanocobalamin
Capillary Fusion Method	>300°C	300 - 302°C

RESULT OF ANALYSIS:

Determination of absorption maxima (λ_{max}):

A stock solution of cyanocobalamin at a concentration of 1000µg/ml was prepared using phosphate buffer at pH 6.8. This sol. was then diluted with same buffer to obtain a conc. of 100µg/ml. The resulting solution was scanned in wave-length range of 400–800nm using a UV-visible spectrophotometer. The λmax of cyanocobalamin in phosphate buffer at pH 6.8 was found to be 522nm.

Determination of Calibration Curve:

Cyanocobalamin was subjected to spectrophotometric measurement using a double beam UV spectrophotometer (UV-1800, Shimazdu, Japan).

Standard calibration curve of Cyanocobalamin in phosphate buffer 6.8 pH:

Table.3.3: Calibration curve of Cyanocobalamin in phosphate buff. pH 6.8 at λmax 522nm

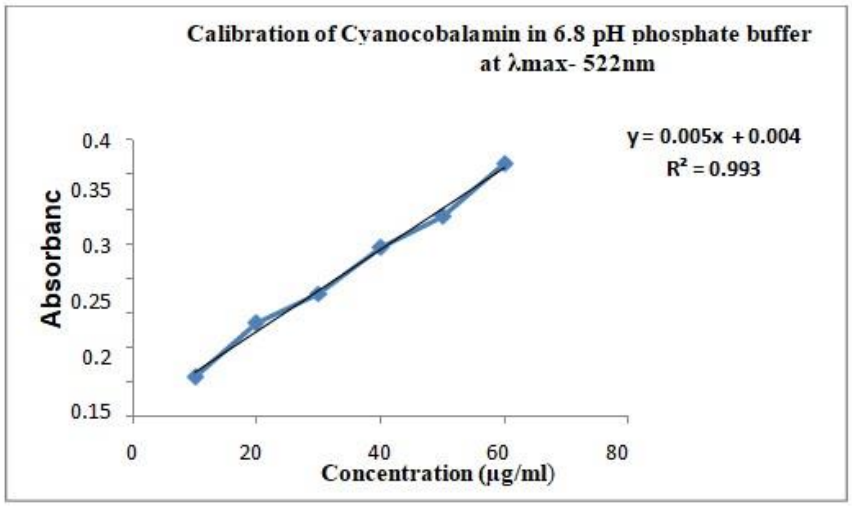

Fig 1: Cyanocobalamin calibration curve in phosphate buffer 6.8 pH at λmax-522 nm

Solution Properties:

Table 4: Solubility study of Cyanocobalamin

Sr. No.	Solvents and buffer	Results
1.	Acetonitrile	Partially soluble
2.	Ethanol	10mg/ml
5.	Dimethyl Sulfoxide	75mg/ml
6.	Water	50mg/ml

Excipients Compatibility Studies:

Sample FTIR Spectra Cyanocobalamin:

The FTIR spectrum of Cyanocobalamin which is performed by FTIR instruments is given as following and the interpretation of Cyanocobalamin was found to be:

Fig.4.3: FT

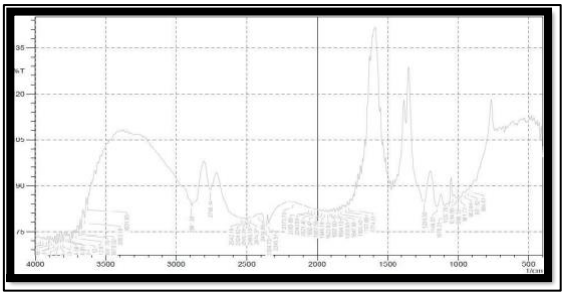

Fig 2: F.T.I.R. Spectra of (Cyanocobalamin+ HPMC):

Partition Co-efficient (Log P) with different Solvents (Aqueous & Non Aqueous):

Log P represents the drug's conc. in both organic (non-aqueous) & aqueous phases. To determine partition co-efficient of cyano-cobalamin in h2o, equal volumes of water as an aqueous phase & non-aqueous as an oil phase were utilized.

$$Po/w = (Coil/Cwater)$$

Partition Coefficient (Log P) with H2O & Chloroform:

Partition coefficient is determined by the following solvents with both Aqueous & Non Aqueous phase.

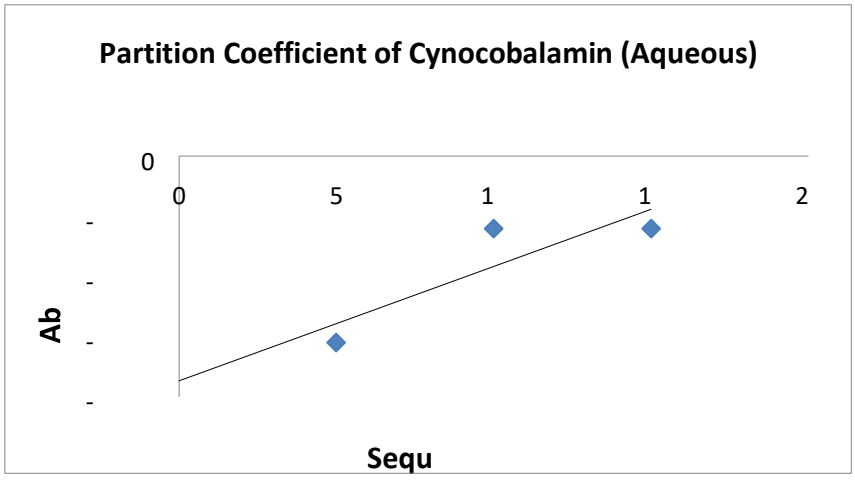

Fig.3: Aqueous Phase (Water) Curve

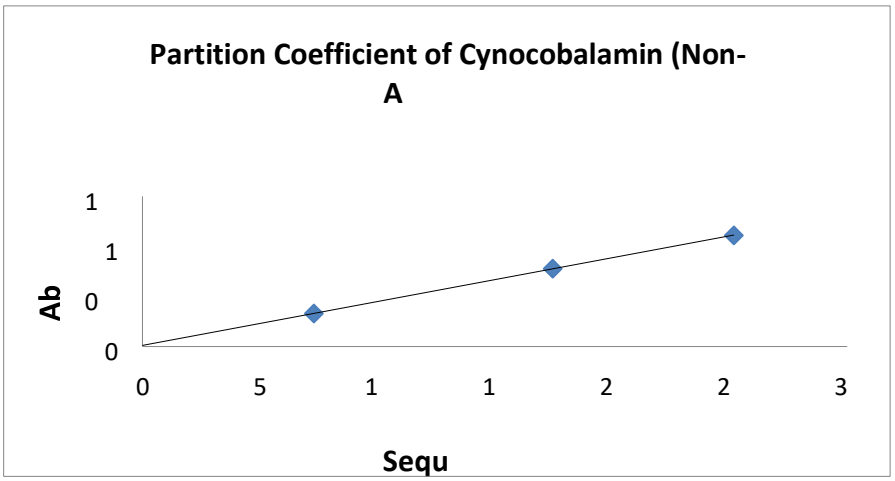

Fig. 4: Non-Aqueous Phase (Chloroform) Curve

Partition Coefficient (Log P) with Water &Iso-Octanol:

Partition coefficient is determined by the following solvents with both Aqueous & Non Aqueous phase.

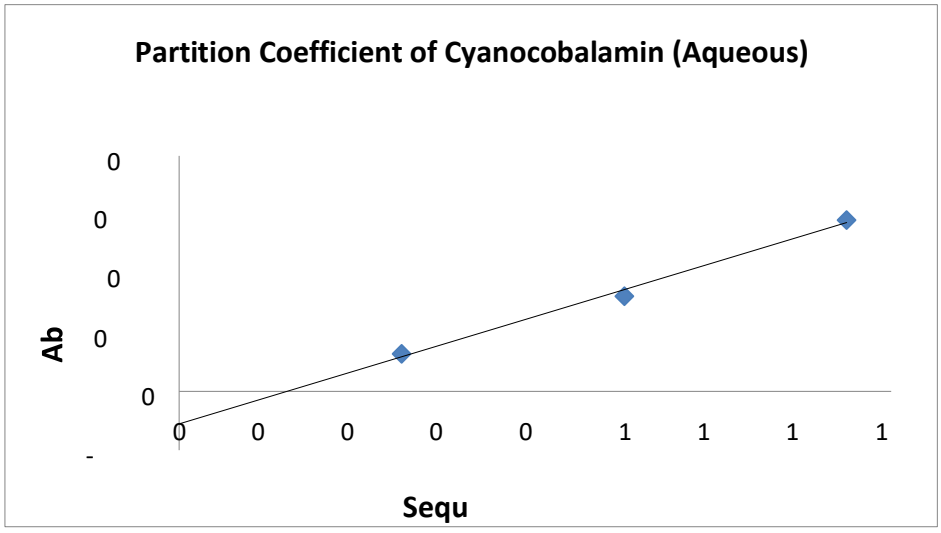

Fig. 5: Aqueous Phase (Water) Curve

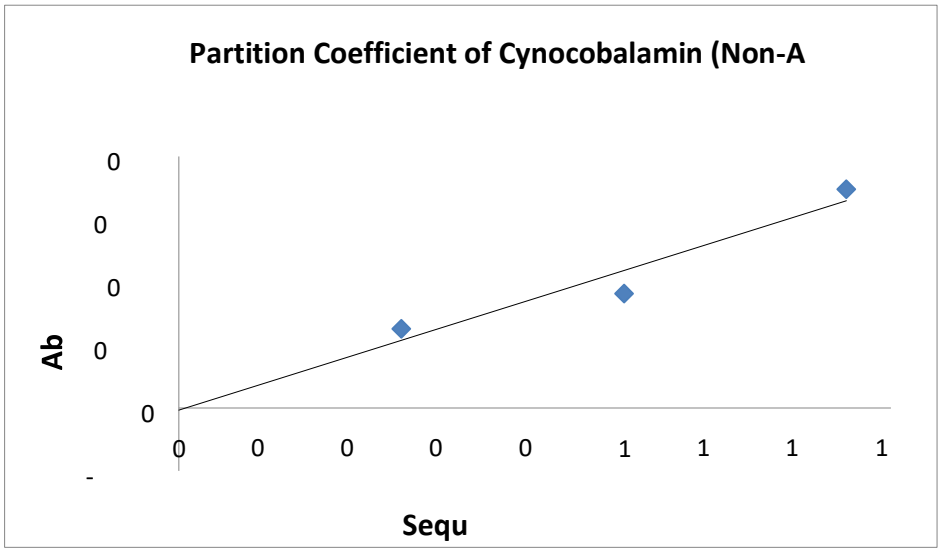

Fig. 6: Non-Aqueous Phase (Iso-Octanol) Curvve

Optimization Pre- compression Parameters of Powder Mixture:

Bulk Density:

Table 5: Bulk Density of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	0.55	0.52	0.58	0.62	0.55	0.53
2.	0.59	0.56	0.54	0.58	0.58	0.52
3.	0.58	0.54	0.55	0.60	0.57	0.56
4.	0.60	0.56	0.56	0.59	0.58	0.51
5.	0.56	0.52	0.57	0.60	0.59	0.54
6.	0.60	0.54	0.56	0.61	0.61	0.58
Mean ± S.D.	0.58±0.021	0.54±0.017	0.56±0.014	0.60±0.014	0.58±0.021	0.54±0.026

Tapped Density:

Table 6: Tapped Density of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	0.70	0.66	0.68	0.72	0.63	0.60
2.	0.73	0.64	0.66	0.68	0.67	0.61
3.	0.71	0.65	0.64	0.70	0.64	0.60
4.	0.69	0.66	0.67	0.69	0.65	0.59
5.	0.72	0.65	0.68	0.67	0.66	0.58
6.	0.71	0.64	0.63	0.68	0.65	0.62
Mean ± S.D.	0.71±0.014	0.65±0.008	0.66±0.020	0.69±0.017	0.65±0.014	0.60±0.014

Angle of Repose: - (tanϴ)

Table 7: Angle of repose of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	27°41”	24°47”	22°62”	26°37”	23°14”	22°74”
2.	26°32”	23°51”	22°35”	25°78”	23°20”	23°11”
3.	27°31”	24°32”	23°11”	26°29”	23°33”	22°68”
Mean ± S.D.	27°01”±0.602	24°10”±0.516	22°69”±0.385	26°14±0.320	23°2±0.097	22°84”±0.232

Carr's Index: It is expressed in Percentage (%) and expressed by;

Table 8: Carr's index of Cyanocobalamin Extended Release Tablet

S.No.	F-1	F-2	F-3	F-4	F-5	F-6
1.	21.42	21.21	14.70	13.88	12.69	11.66
2.	19.17	12.50	18.18	14.70	13.43	14.75
3.	18.30	16.92	14.06	14.28	10.93	6.66
4.	13.04	15.15	16.41	14.49	10.76	13.55
5.	22.22	20.0	16.17	10.44	10.60	6.89
6.	15.49	15.62	11.11	10.29	6.15	6.45
Mean ± S.D.	18.30±3.5 0	16.92±3.2 3	15.15±2.4 2	13.04±2.0 6	10.76±2.5 3	10.0±3.7 7

Hausner's Ratio:

Table 9: Hausner's Ratio of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	1.27	1.26	1.17	1.16	1.14	1.13
2.	1.23	1.14	1.22	1.17	1.15	1.17
3.	1.22	1.20	1.16	1.16	1.12	1.07
4.	1.15	1.17	1.19	1.16	1.12	1.15
5.	1.28	1.25	1.19	1.11	1.11	1.07
6.	1.18	1.18	1.12	1.11	1.06	1.06
Mean±S.D.	1.22±0.05 0	1.20±0.04 6	1.17±0.03 3	1.15±0.02 7	1.12±0.03 1	1.11±0.04 7

Optimization Post- Compression Parameters:

Wt. Variation:

Table 10: Wt. variation of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	302	304	300	302	305	308
2.	308	306	304	300	308	300
3.	304	301	303	304	308	301
4.	303	300	307	306	306	309
5.	302	308	309	304	304	303
6.	308	306	301	305	302	304
7.	303	308	306	300	304	301
8.	334	306	308	310	300	399
9.	399	301	304	305	307	300
10.	300	304	303	304	306	307
Mean±S.D	303±2.94	304±2.91	304±2.95	204±2.94	305±2.58	303±3.64

Thickness: (mm.)

Table 11: Thickness of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	4.81	4.84	4.72	4.78	4.84	4.82
2.	4.78	4.81	4.76	4.74	4.81	4.86
3.	4.74	4.72	4.84	4.80	4.74	4.84
4.	4.84	4.78	4.80	4.81	4.71	4.78
5.	4.80	4.87	4.84	4.83	4.84	4.76
6.	4.76	4.88	4.86	4.87	4.86	4.80
7.	4.74	4.78	4.81	4.80	4.78	4.78
8.	4.85	4.80	4.74	4.72	4.76	4.81
9.	4.77	4.72	4.81	4.80	4.79	4.83

10.	4.79	4.74	4.84	4.81	4.85	4.77
Mean±S.	4.78±0.0	4.79±0.0	4.80±0.0	4.79±0.0	4.7±0.05	4.8±0.03

Hardness:

Table 12: Hardness of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	1.8	2.1	2.7	2.6	3.0	3.4
2.	1.7	2.4	2.9	2.9	3.1	3.7
3.	1.4	2.2	3.0	2.6	3.3	3.8
4.	1.5	2.1	2.8	2.8	3.1	3.5
5.	1.8	2.8	2.6	2.9	3.4	3.4
6.	1.6	2.5	2.7	2.7	3.2	3.3
7.	1.4	2.6	2.8	2.8	3.3	3.6
8.	1.6	2.5	2.7	2.8	3.2	3.5
9.	1.5	2.4	2.8	3.0	3.3	3.7
10.	1.4	2.7	2.5	3.1	3.4	3.8
Mean±S.D	1.57±0.15	2.43±0.24	2.75±0.14	2.82±0.16	3.23±0.13	3.57±0.17

% Friability:

Table 13: % Friability of Cyanocobalamin Extended Release Tablet

S.NO.	F-1	F-2	F-3	F-4	F-5	F-6
1.	1.16	1.04	0.94	0.74	0.68	0.51
2.	1.19	1.07	0.92	0.78	0.67	0.54
3.	1,21	1.08	0.89	0.80	0.69	0.53
4.	1.14	1.05	0.94	0.76	0.68	0.55

5.	1.15	1.04	0.96	0.77	0.65	0.49
6.	1.17	1.09	0.91	0.75	0.70	0.52
Mean±S.D.	1.17±0.026	1.06±0.021	0.92±0.025	0.76±0.021	0.67±0.017	0.52±0.021

Drug Content:

Table 14: % Drug Content of Cyanocobalamin Extended Release Tablet

Formulations	Assay-1 (mcg)	Assay-2 (mcg)	Assay-3 (mcg)	Mean±S.D. (mcg)	% Drug Content
F-1	1501	1497	1504	1504±0.010	100.26
F-2	1501	1505	1484	1496±0.020	99.73
F-3	1511	1480	1512	1501±0.015	100.06
F-4	1504	1495	1508	1497±0.026	99.80
F-5	1490	1509	1506	1502±0.020	100.13
F-6	1495	1488	1504	1495±0.025	99.66

% Drug-Content (Assay) Graphs of Formulation (F-5) by HPLC:

% Drug-content of Cyanocobalamin Extended Release Tablet by UV-VIS Spectroscopy is given as well as following; in all formulations graphs, first 3 point which is having sequence no 2, 3, & 4 are showing the absorbance results of standard of Cyanocobalamin & similarly all point except standard point showing the absorbance result of sample of Cyanocobalamin Extended Release Tablet.

In-vitro Drug Release Study:

The type-1 dissolving device was used for in-vitro dissolution. Extended Release Cyanocobalamin is listed in table. The F5 formulation of these Extended Release tablets was determined to be best as it had a 100% drug release in 12hours. Compared to other formulations, medicine is released significantly more effectively by formulation that contains polymer (HPMC).

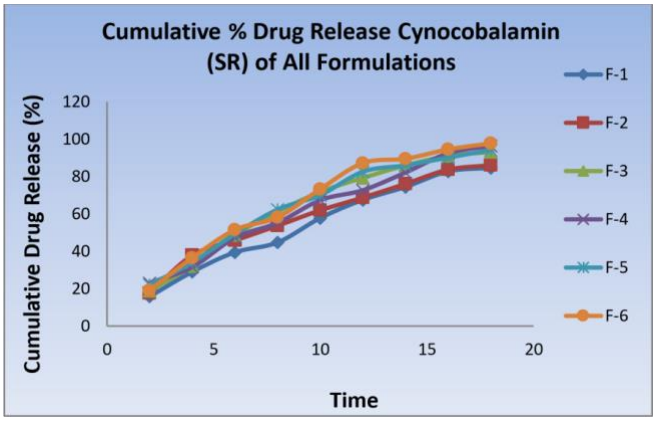

Fig. 7: Cumulative % Drug release of all formulation

Release Kinetic Analysis:

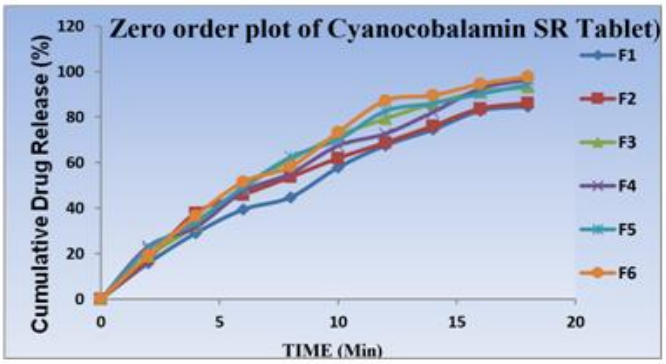

Fig. 8: Zero order release kinetic plot from F_1 to F_6 formulations of Tablet.

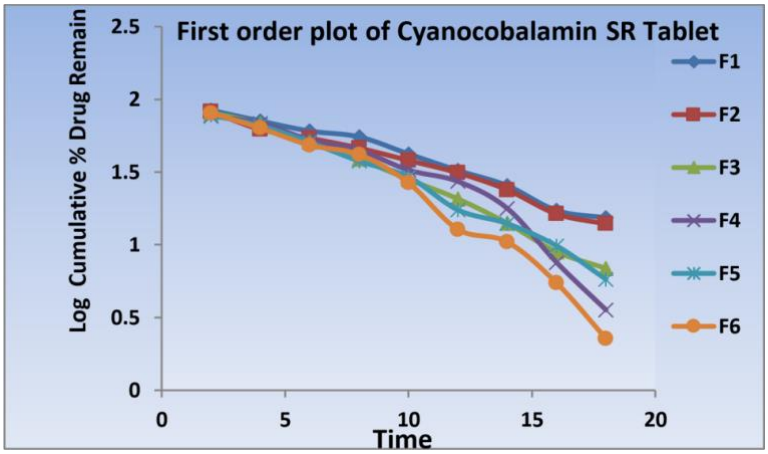

Fig. 9: 1st order release kinetic plot F_1 to F_6, formulations of Tablet.

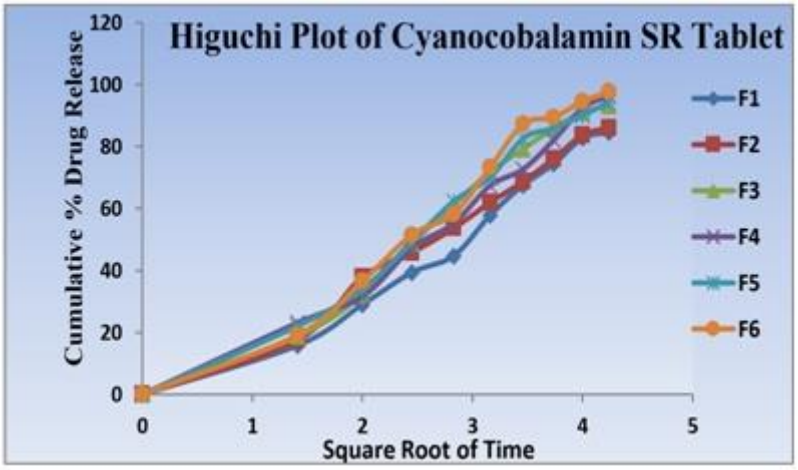

Fig. 10: Higuchi release kinetic F_1 to F_6 formulations of Tablet

Korsmeyer Peppas release kinetic plot:

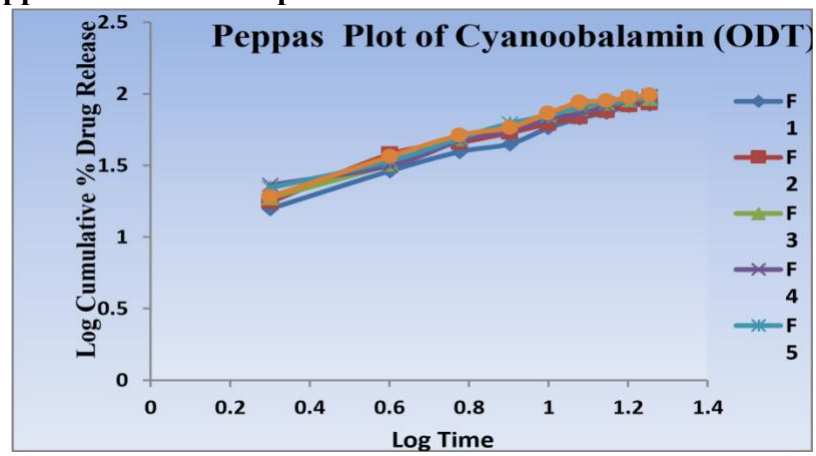

Fig. 11: Korsmeyer Peppas kinetic $F_{1, 2, 3, 4, 5}$ & F_6 formulations of Tablet

Stability Studies:

Table 15: Stability study of optimized formulation (F-5)

Parameter	Initial	After-1M	After-2M	After-3M
Colour	Dark Red Colour	No change	No change	No change
Size & Shape	9.6mm in size	-	-	-
Weight Variation (mg)	308.3±2.43	306.2 ±2.09	308.6 ± 2.59	307.7 ± 2.16

Thick-ness (mm)	4.81 ±0.044	4.82 ± 0.034	4.82 ± 0.033	4.81 ± 0.028
Hard-ness (kg/cm^2)	4.8 ± 0.110	4.9 ± 0.166	4.8 ± 0.157	4.9 ± 0.164
% Friability	0.30 ±0.020	0.31 ± 0.014	0.32 ± 0.021	0.30 ± 0.024
Drug-Content (%)	99.75±0.01	99.69 ±0.03	99.71 ± 0.02	99.65 ± 0.03

Discussion:

Extended Release tablets of Cyanocobalaminis prepared because it help in getting maximum amount of drug from mouth pharynx as these are sites for maximum absorption of drug.

Identification of drug purity was done through FTIR. The optimization formulation, of pure drug was subjected to FTIR analysis. No major difference was observed in FTIR spectra of pure drug & other materials which are used for medicated formulation, indicating FTIR of drug was concluded to be pure as it was found to match with reference FTIR of Cyanocobalamin. Drug- polymer interaction was ruled out as there was no major shift in absorption bands (Peaks) of Cyanocobalamin in present of polymer combinations. The various formulations varies between 0.52-0.60 (gm/ml), 0.55-0.70 (gm/ml) & 22-30. The Carr's index of various formulation were varies between 9.50-20.00 %. The Hausner ratio of various formulations also varies between 1.00- 1.30 %. According to the post compression parameter of all formulations are given as well as following. In the formulation the hardness of all formulations were varies between **NLT 2.0 (kg/cm^2).**

Wt. variation was found within specification of (IP 2010) Twenty tablets from each formulation had an average tablet percentage deviation that was kept within 7.5%. The weight variation of the various formulations was varied between 300-305mg. The Thickness of the various formulations was varied between 4.50-4.80mm. A range of NMT 1.0% was discovered for the friability of the chosen formulations. All formulations' medication contents were found to be between 97.0 and 100.0%. The ability of a formulation to stay within a specified range is typically used to characterize a preparation's stability. Oral administration of dosage form should lead to appropriate distribution and show the activity of therapeutic moiety depending on the characteristic of dosage form and drug. Among these formulated Extended Release

tablets of Cyanocobalamin, **Formulation (F-5)**was determined to be the best since the drug's 12-hour release was NLT 90.0%.

RESULT

All the formulations were subjected to physical stability testing program, under different stress condition to study effect of temp. & humidity as per guidelines. The observation were made in respect of change in colour, size & shape, wt. variation, hard-ness, thick-ness, % friability, disintergration time, % drug content. It is evident that most of Sustained Release tablets of Cyanocobalamin HCl were unaffected in respect of respect colour, size & shape stability after storage for 3-months. No appreciable change in physical characteristic, wt. variation, hard-ness, thick-ness, % friability, % drug content & in-vitro drug release amount was observed even after evaluation for 3-months' storage. Stability studies exhibited that prepared tablets are quite stable at storage condition that is at 40°c ± 2°c temperature (75±5% RH).

REFERENCES

1. Ali J, Khar RK, Ahuja A. A Textbook of Biopharmaceutics & Pharmacokinetics. Birla Publications Pvt. Ltd. Delhi. 2008; 252-72.
2. Anwar Ma'ali; Naseef H, Qurt M, Abukhalil AD, Rabba AK, Sabri I. The Preparation and Evaluation of Cyanocobalamin Mucoadhesive Sublingual Tablets. Pharmaceuticals. 2023; 16(10): 1412.
3. Basak SC, Reddy JBM, Lucas Mani KP. Formulation and release behaviour of Extended Release Cyanocobalamin hydrochloride HPMC Matrix tablet. Indian Journal of Pharmaceutical Sciences. 2006; 68(5): 594-598.
4. Brahmankar HA, Jaiswal SB. Biopharmaceutics and Pharmacokinetics: A Treatise. VallabhPrakashan. 2000: 337, 348-357.
5. Borguist P, Korner A, Larsson A. A model for the drug release from polymeric matrix tablets: effect of swelling and dissolution. J Controlled Release. 2006; 113(3): 216-225.

6. Rajput A, Verma A, Himani K, Singh MK, Kumar B. DEVELOPMENT AND EVALUATION OF NATURAL SUPERDISINTEGRANT-BASED ORODISPERSIBLE TABLETS OF LOSARTAN POTASSIUM FOR MANAGEMENT OF HYPERTENSION. Journal of Advanced Pharmaceutical Sciences and Natural Products. 2026 Jan 19;1(1).
7. Chandran S, Laila FA, Mantha N. Design and evaluation of Ethyl Cellulose Based Matrix Tablets of Ibuprofen with pH Modulated Release Kinetics. Indian Journal of Pharmaceutical Sciences. 2008; 42(5): 234-240.
8. Chen X, Wen H, Park K. Challenges and new technologies of oral controlled release. Oral Controlled Release Formulation Design and Drug Delivery: Theory to Practice. 2010; 257-277.
9. Chien YW. Rate controlled drug delivery systems. 2nd ed. Marcel Dekker; New York, Revised and expanded. 2005; 2: 1-10.
10. Rajput A, Himani K, Verma A, Singh MK, Kumar B. ORODISPERSIBLE TABLETS AS MODERN ORAL SOLID DOSAGE FORMS. Journal of Advanced Pharmaceutical Sciences and Natural Products. 2026 Jan 19;1(1).
11. Garg A, Rathor M. Tablet Evolution: Exploring Cutting-edge Technologies in Formulation and Development. Asian Journal of Pharmacy and Technology. 2024 Dec 21;14(4):373-8.
12. Eisai Submits New Drug Application for Mecobalamin Ultra-High Dose Preparation as Treatment for Amyotrophic Lateral Sclerosis in Japan. (PDF) Eisai.com. Retrieved 28 January 2018.
13. GadadeVaibhav, Ganesh Rasal, D. shivarkar Preparation and Evaluation of Sustained Release Tablet of Cyproheptadine Hydrochloride Using Carbopol and HPMC The Pharma Innovation – Journal Vol. 2 No. 1 2013.
14. Sharma S, Verma A, Kumar B. ORAL DRUG DELIVERY SYSTEMS WITH EMPHASIS ON EXTENDED AND SUSTAINED RELEASE MECHANISMS: A REVIEW. Journal of Advanced Pharmaceutical Sciences and Natural Products. 2026 Jan 19;1(1).
15. Chauhan R, Verma A, Singhal T, Garg A, Kumar B, Pandey D. Design And Evaluation Of Teneligliptin Tablet: Teneligliptin Tablet. INDONESIAN JOURNAL OF HEALTH SCIENCES RESEARCH AND DEVELOPMENT (IJHSRD). 2023 Jun 27;5(1):89-100.