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DESIGNING OF FORMULATION OF SUSTAIN RELEASE TABLET OF TACROLIMUS WITH COTRIMAXAZOLE

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A B S T R A C T

The Tablet Helps to Achive

1. A single tablet for three medicines
2. A single tablet for three complications
3. Comparatively less medication after organ transplant
4. Reduces the chance of infection after organ transplant
5. Drug category: immunosuppressant and antibiotic
6. To reduce the frequency of drug intake
7. To reduce chance of drug - drug interaction

To do so following consideration is to be kept in mind during formulation

1. Tablet drug content should be potent to their action.
2. To reduce chance of drug – drug interaction
3. To increase bioavailability and effectivity
4. Selection of best combination of immunosuppressant with suitable antibiotic.

Keyword: Tablet Of Tacrolimus with Cotrimaxazole

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INTRODUCTION

The first successful kidney transplant was performed by Dr. Joseph Murray, a plastic surgeon, in 1952. Since that time, significant advances in transplant surgery and immunologic research led to longer lives for solid organ transplant recipients (SOTRs). Resultant improved quality of life led to increased demand for plastic and reconstructive surgery in SOTRs. One common indication for surgical management in SOTRs is squamous cell carcinoma, which presents more frequently and at more advanced stage in SOTRs. In 2012, over 28,000 organ transplants were performed in the United States. Long-term survival of solid organ transplant recipients (SOTRs) has increased dramatically due to advancements in surgical technology and immunosuppressive therapies. Bacteria are the leading cause of infections after solid organ transplantation. In recent years, a progressive growth in the incidence of multidrug-resistant (MDR) and extensively-drug-resistant (XDR) strains has been observed. While methicillin-resistant Staphylococcus aureus (MRSA) infection is declining in non-transplant and SOT patients worldwide, vancomycin-resistant enterococci, MDR/XDR Enterobacteriaceae and MDR/XDR non-fermenters are progressively growing as a cause of infection in solid organ transplant (SOT) patients and represent a global threat. As the antibiotics active against MDR bacteria have several limitations for their use, which include less clinical experience, higher incidence of adverse effects and less knowledge of the pharmacokinetics of the drug, and, in most cases, are only available for parenteral administration. Manufacturing of tablet and syrup are usual in pharmaceutical field, all most all times patient need to take many tablet for different reason at a time or at a gap of certain period. It is difficult in case of pediatric patient to give many tablets as they generally refuse to take such therapy.[1]

Tablets are the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease in manufacturing. Tablet disintegration has been considered as the rate limiting step in faster drug release. Developing a solid oral dosage form in today's market can be challenging. There are many pressures to discover new entities and maximize the lifecycle of products while maintaining safety, cost-effectiveness, and speed to market Tablets are almost certainly the most cost-effective. And efficient form of dispensing medicines. Tablet provides a versatile, compact, robust and accurate platform for drug delivery. While the functional versatility of the tablet as a dosage form has been appreciated for decades, the design versatility of the tablet has historically been underappreciated One of the approach to increase gastric residence time is by gastroreten.

- Many times, patient miss the drug dose to be taken due to work load or forgetness.
- Due to busy schedule especially at the afternoon time, where they get hardly time for lunch.
- Patient has to take number of drugs, when he suffers from fever, in such condition patient has to take a single drug and over.
- Tablet becomes economical to patient and even to manufacturer.

Here we have tried to make compatible formulation with each other such that drug release profile should reach to maximum in a controlled condition.

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Various formulations have been developed and tried to incorporate combination of polymer so that the best formulation can be developed.

At least 90% of drug used to produce systemic effect are administered by oral route. Tablet are intended for oral administration, some are swallowed whole, some are being chewed, some are dissolved or dispersed in water before being and some are retained on mouth, where the active ingredients are liberated. Tablets are used for systemic effect drug delivery. For systemic use drug must be released from tablet that dissolve in fluid of mouth, stomach and intestine and then absorbed into systemic circulation by which it shows its therapeutic effect.

Resultant improved quality of life led to increased demand for plastic and reconstructive surgery in SOTRs. One common indication for surgical management in SOTRs is squamous cell carcinoma, which presents more frequently and at more advanced stage in SOTRs. Few studies investigate outcomes of surgeries performed on SOTRs after transplantation. Case reports describe individual instances of surgery performed on SOTRs. Case series assessing safety of plastic surgery in SOTRs, including free flap reconstruction, found no definitive contraindication to performing these procedures in carefully selected SOTRs. In US a 2009 nationwide survey, 25% of responding plastic surgeons reported they performed plastic surgery procedures in SOTRs with an extremely low complication prevalence based on self-report.

Within transplant medicine, the risk of allograft rejection is one of the major hurdles that must be overcome. In recent years, there has been an increase in the survival rates of solid organ transplant recipients due to advancements in organ procurement, surgical methods, and immunosuppressive therapy. Despite this progress, transplanted organs still experience injury caused by immune and non-immune related factors that include rejection due to infiltrating immune cells or antibodies against donor specific epitopes in the transplanted organ, viral infection, and drug toxicity due to the long-term use of immunosuppressive drugs. Part, if not the majority of this injury is caused by immune and non-immune related factors and can be avoided by the timely detection of such events in their early stage. Current diagnostic approaches lack the necessary sensitivity and selectivity required to accurately identify these events early enough so that the damage to the transplanted organ or “graft” can be avoided.

Early identification of allograft injury not only allows for timely intervention but can also be used for patient-specific customization of immunosuppressive drugs to optimize graft outcome. Understanding the correlation between their presence or lack thereof also offers insight into post-transplant graft monitoring. Early detection of rejection events in conjunction with intervention is therefore the key to the prevention of acute rejection and other subsequent injuries, which can occur within the first few years after transplantation.[2]

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EXPERIMENTAL WORK

1. PRE - FORMULATION STUDIES

1.1 Organoleptic Properties:

1.1.1 Colour

A small quantity of active drug powder was taken in butter paper and viewed in well illuminated places.

1.1.2 Odour

Very less quantity of active drug powder was used and smelled to get the odour.

2. CHARACTERIZATION STUDY

2.1 Peak Identification by HPLC

For Tacrolimus: The HPLC assay was carried out using an Agilent Eclipse XDB-C8 column (5 μm,4.6 mm×150 mm) where the column temperature was 50 and detection wavelength was 210 nm, and the mobile phase was 50% acetonitrile and 50% monobasic potassium phosphate buffer (0.05 mol·L-1), which contained 0.2% polyoxymethylene lauryl ether (Brij35) with pH adjusted to 3.0±0.1 with phosphoric acid. The flow rate was 1.5 mL per minute. The test solution of tacrolimus was prepared with a mixture of water and acetonitrile (1:1), incubated for 3 hours at ambient temperature to allow the dynamic equilibrium of three stereo-isomers of tacrolimus.

For sulphamethoxazole and trimethoprim: Preparation of Mobile Phase: Prepare, filtered and degassed mixture of buffer and Acetonitrile in the ratio of 30:70 v/v. Preparation of Standard solution: Accurately weighed and transferred about 50mg of sufamethoxazole and 10mg of Trimethoprim working standard into a 10ml volumetric flask add 2ml of mobile phase, sonicated for 15min and make up to the mark with mobile phase. Preparation of Sample solution: Crush 20 tablets and transferred accurately weighed powder equivalent to 50mg of Sulfamethoxazole and 10mg of Trimethoprim into 10ml volumetric flask add 7ml of mobile phase sonicate for 20min to dissolve and make up to the volume with mobile phase. Filter the solution through 0.45μm nylon filter. Transfer 0.1ml of above solution into 10ml volumetric flask and make up to the volume with mobile phase (50ppm of sulphamethoxazole & 10ppm of trimethoprim).

3. PROCEDURE FOR EVALUATION OF GRANULES PARAMETERS

3.1 Flow Properties

3.1.1 Angle of Repose

Angle of repose is an indicative of the frictional forces existing between the particles. It is defined as the maximum angle possible between the surface of the pile of powder and the horizontal plane.

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$$\text{Tan } \theta = h/r$$

$$\theta = \tan^{-1} (h/r)$$

Where: θ = angle of repose, h = height of the heap of powder in cm, r =radius.

Value of θ are rarely less than 20° and values up to 40° indicates good flow potential.

Method

A funnel was fixed at a particular height 'h' cm on a burette stand. A graph paper was placed below the funnel on the table. The given powder whose angle of repose is to be determined passed slowly through the funnel, until it forms a pile. Care is taken to see that the drug particles slip and roll over each other through the sides of the funnel. Further addition of the powder is stopped as soon as the pile touches the tip of the funnel. Circumference of the pile is drawn with pencil without disturbing the pile. The radius of the pile is noted as 'r' cm. Angle of repose θ of the granules is then calculated from the above formula.

Table No. 1: Flow Properties and Corresponding Angle of Repose

Flow Properties	Angle Of Repose
Excellent	25-30
Good	31-35
Fair aid may hang up	36-40
Poor must agate, Vibrate	41-45
Very poor	46-55
Very, very poor	>66

3.1.2 Bulk density (p_b)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and the volume was noted. It is expressed in gm/ml and is given by;

$$Pb = \frac{M}{V_b}$$

Where: M is mass of powder, V_b is the Bulk volume of the powder

Method

Accurately weighed quantities of the powders (5gm) were carefully poured into the graduated cylinder through a large funnel and the bulk volume was noted with and without taping. Bulk and tapped densities were calculated from the following formula, weight / untapped or initial volume and weight / tapped volume, respectively.

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3.1.3. Taped Density

The granules sample was poured gently through glass fumed into graduated measuring cylinder. Initial volume of powder was noted and the sample subjected to tapping (500, 750 or 1250 Tapping) until to further reduction in volume was noted or the percentage of difference in volume was not more than 2% Volume occupied the samples after tapping was recorded and tapped density was calculated using following formula.

$$\text{Tapped density} = \frac{\text{Weight of sample in gm}}{\text{Volume after tapping}}$$

3.1.4 Compressibility

An important measure that can be obtained from bulk density determination is the percent compressibility, which is defined as:

$$C = \rho t - \rho b / \rho t \times 1$$

Where: ρb = bulk density

ρt = tapped bulk density

In theory, the less compressible a material means, the more flow able it is. A material having a C value of less than 20% is defined as free-flowing powder.

3.1.5. Hauser's Ratio

It is the ratio of bulk volume to tapped volume or tapped density to bulk density.

Hausner's Ratio = ρt / ρb

Where: ρb = bulk density

ρt = tapped bulk density

Table No. 2: Scale Of Flowability by Hausner's Ratio

Limits of Hausner's Ratio	Category
1.2 – 1.3	Excellent
1.3– 1.4	Good
1.4 – 1.5	Fair
1.5 -1.6	Poor

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4. PREPARATION OF STOCK SOLUTION FOR STANDARD CALIBRATION CURVE

4.1. Preparation Of Stock Solution for Tacrolimus

1mg of Tacrolimus was dissolved in 10 mL of methonolic phosphate buffer pH 6.8 to get 100 µg/mL solutions.

4.1.1. Development of Standard Calibration Curve of Tacrolimus

From the above stock solution 1ml, 2ml, 3ml, 4ml, 5ml and 6ml were pipetted out and made up to 10ml by using distilled water in standard flasks to produce 10, 20, 30, 40, 50 and 60 µg/ml respectively. The absorbance was measured at 297nm in a UV spectrophotometer using distilled water as blank. The data's were tabulated. The concentration was plotted against absorbance.

4.2 Preparation of Stock Solution of Sulphamethoxazole

Solution of 1000 µg. mL-1 sulfamethoxazole was prepared by dissolving accurate weighted 0.100 g of pure drug in 10 mL of 0.4 M HCl and further diluted to the mark in volumetric flask 100 mL with distilled water and stored in a cool (<25 ºC) and dark place.

4.2.1 Development of Standard Calibration Curve of sulphamethoxazole:

The concentration of sulfamethoxazole (SMX) in calibration curve was 750 ng/mL, 2080 ng/mL, 3330 ng/ mL, 4170 ng/mL, 5 µg/mL, 5833 ng/mL, 6670 ng/mL for SMX.

4.3 Preparation of Stock Solution of Trimethoprim

Primary stock solutions consisted of trimethoprim (0.32 mg/mL) were prepared in methanol. Trimethoprim stock solution was further diluted with mobile phase to obtain different concentration.

4.3.1 Development of Standard Calibration Curve of trimethoprim

The concentration of trimethoprim (TMP) in calibration curve was 150 ng/mL, 420 ng/mL, 670 ng/mL, 830 ng/mL, 1000 ng/mL, 1170 ng/mL, 1330 ng/mL for TMP.

The dilution was analyzed for absorbance at 297 nm using a UV-visible spectrophotometer (shimandzu, JAPAN). The calibration curve was obtained in accordance with Beer- Lambert law.

5. PREPARATION OF SUSTAIN RELEASE TABLETS BY WET GRANULATION METHOD

The sustain release tablets were prepared by conventional wet granulation technique. The composition with respect to polymer combination was selected on the basis of trial preparation of tablets. In each formulation, the amount of the total weight of a tablet is about 1000 mg. A batch of 50 tablets was prepared with each formula. The ingredients were passed through a 60-mesh sieve. A blend of all ingredients except glidant and lubricant was mixed, a particular attention had been given

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to ensure thorough mixing and phase homogenization. Granulation was done manually with a solution of water. The wet masses were passed through a 12-mesh sieve and the wet granules produced were first air dried for 10 min and finally at 45-50° in a tray drier for 2 h. The dried granules were sized by a 16-mesh sieve and after lubrication with magnesium stearate. Compression was carried out using 8 mm flat faced circular punches into tablets on an multi station rotary tablet compression machine at a constant compression force. Just before compression, the surfaces of the die and punches were lubricated with magnesium stearate. All the tablets were stored in airtight close containers for further tests.

6. PROCEDURE FOR EVALUATION OF TABLETS

The tablets were compressed using 8mm diameter, round, biconcave punches on a multistation rotary tablet machine. The tablet weight was kept about 1000 mg and hardness between 6–7 kg/cm2. Other parameters like size, thickness, shape, hardness, friability, weight variation, wetting time were carried out.

6.1 Thickness and Shape

Size (diameter) and thickness was measured using Vernier Caliper.

Method

Ten tablets from each formulation were selected and their crown thickness was measured with a Vernier Calliper. Shapes of the tablets were observed.

6.2 Hardness

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacturing, packing and shipping.

Method

The Monsanto hardness tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet and zero reading is taken. The upper plunger is then forced against a spring by turning threaded bolt until the tablets break. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of break was recorded and zero force reading is deducted from it.

6.3 Friability

Tablets were tested for friability using Electrolab Friabilator. This is important to know the mechanical strength of the tablet while handling.

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Method

Twenty tablets were weighed initially and transferred to the Friabilator. The instrument was set to 25 rpm for 100 rotations. The resulting tablets were reweighed and percentage loss was calculated using the formula.

$$F = \frac{\text{Initial weight} - \text{Final weight}) \times 100}{\text{Initial weight}}$$

6.4 Weight Variation

Weight variation was determined to know whether different batches of tablets have uniformity.

Method

Weighed 20 tablets individually, calculated the average weight, and compared the individual tablet weights to the average. The tablets meet the test if not more than two tablets are outside the percentage limit and none of the tablet differs by more than two times the percentage limit. The weight variation tolerance for uncoated tablets differs depending on average weight of the tablets.

6.5 Disintegration Test

The disintegration time was measured using a disintegration apparatus. For this purpose, 6 tablets were filled in vessel containing solvent or water or simulated saliva fluid. The tablet was carefully put in the center of the vessel and the time for the tablet to completely disintegrate into fine particles was noted in respective rotation.

6.6 In Vitro Dissolution Study

The release rate Tacrolimus, sulphamethoxazole and trimethoprim from sustain release dissolving tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 6.8 pH phosphate buffer, at 37± 0.5^0C and 50 rpm. A sample (10mL) of the solution was withdrawn from the dissolution apparatus at 2, 4, 6, 8, 10, 12 hr. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a Watman filter paper. Absorbance of these solutions was measured at 297 nm, 259 nm, 237.6 nm respectively, using a Shimadzu UV-1601UV/Visible beam spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

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6.7 Drug Content: (Procedure for Determining Tacrolimus, Sulphamethoxazole and Trimethoprim in Tablet Formulation)

Tablet Stock Solution:

Twenty tablets were accurately weighed and powdered in a mortar. An amount of powder equivalent to the weight of one quarter of a tablet was mixed with 35ml of ethanol in 100ml - calibrated flasks. The mixture was then sonicated for 15 minutes on an ultrasonic bath and subsequently made up to volume with ethanol, filtered through a Whatman No. 1 filter paper and the filtrate used for preparation of the tablet assay solution.

Tablet Assay Solutions:

The tablet stock solution buffered to pH 4.5 and ethanol were added to produce an assay solution equivalent to sulphamethoxazole 25 μgml^{-1} and trimethoprim 5μgml^{-1}. The D_1-curve of the solutions (n=5) were obtained and sulphamethoxazole and trimethoprim determined as described above.

RESULTS AND DISCUSSION

1. Preformulation Studies for Tacrolimus, Sulphamethoxazole and Trimethoprim

1.1 Organoleptics Properties

Table No.3: Test And Observation of Sulphamethoxazole, Trimethoprim and Tacrolimus

Test	Tacrolimus	Sulphamethoxazole	Trimethoprim
Colour	White powder	White to slightly off-white crystalline powder	White to yellow powder
Odour	Odourless	odourless	odourless
Melting point	169^0C-172^0C	167 - 169^0C	199-203^0C

2. Characterization Study by HPLC

FOR PEAK IDENTIFICATION by HPLC

TACROLIMUS

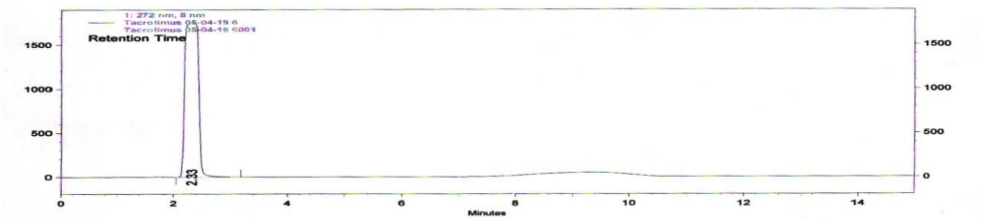

Figure No 1: Peak Of Tacrolimus By HPLC

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TACROLIMUS AND SULPHAMETHOXAZOLE

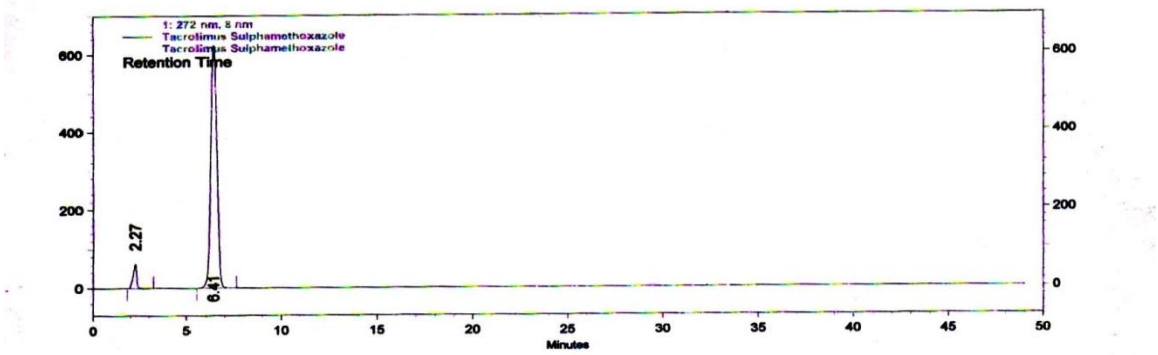

Figure No 2: Peak of Tacrolimus and Sulphamethoxazole by HPLC

TACROLIMUS and TRIMETHOPRIM

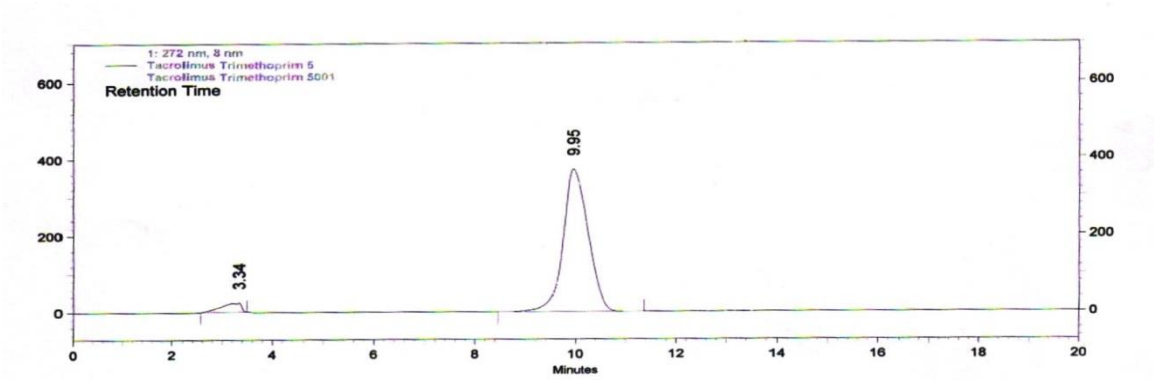

Figure No 3: Pak of Tacrolimus and Trimethoprim by HPLC

TACROLIMUS, SULPHAMETHOXAZOLE and TRIMETHOPRIM

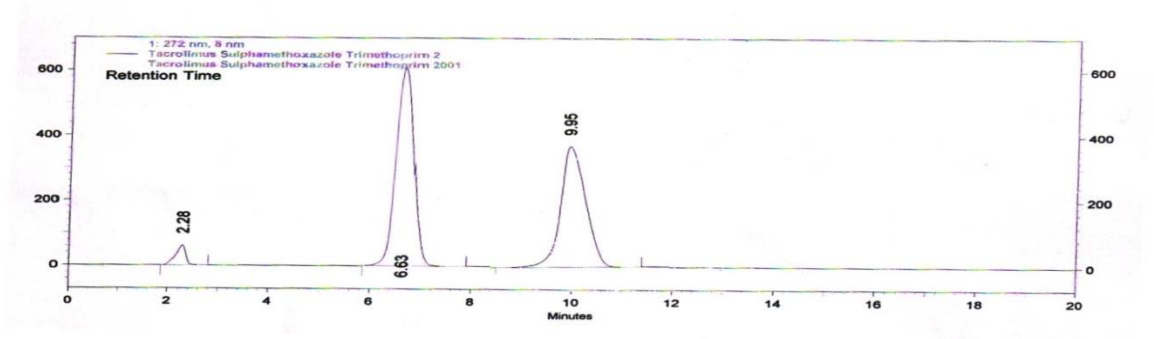

Figure No 4: Peak Of Tacrolimus, Sulphamethoxazole and Trimethoprim by HPLC

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3. Procedure for Evaluation of Granules Parameter

Table No 4: Pre-Compression Parameters of All Formulation (Mean±SD)

Batch	Angle of Repose (θ)	Bulk Density (g/cc)	Tapped Density (g/cc)	Compressibility %	Hausner's Ratio
F1	26.0±0.01	0.65±0.02	0.73±0.03	23.60 ±1.25	1.32±0.03
F2	29.7±0.03	0.59±0.03	0.79±0.03	25.22 ±1.54	1.34 ±0.03
F3	25.1±0.04	0.48±0.03	0.78±0.04	23.61 ±1.32	1.34± 0.02
G4	26.3±0.04	0.53±0.04	0.70±0.02	20.00 ±1.54	1.32± 0.03
G5	27.5±0.03	0.46±0.01	0.71±0.03	19.42 ±1.62	1.25±0.02
G6	30.5±0.05	0.52±0.04	0.67±0.03	21.57 ±1.52	1.29± 0.03
H7	26.5±0.01	0.63±0.03	0.57±0.04	20.64±1.24	1.22±0.02
H8	27.4±0.02	0.61±0.04	0.68±0.03	21.12±1.45	1.24±0.01
H9	29.7±0.03	0.59±0.03	0.79±0.03	25.22±1.54	1.34±0.03

4. ESTIMATION OF TACROLIMUS BY UV SPECTROSCOPY

STANDARD CALIBRATION CURVE OF TACROLIMUS

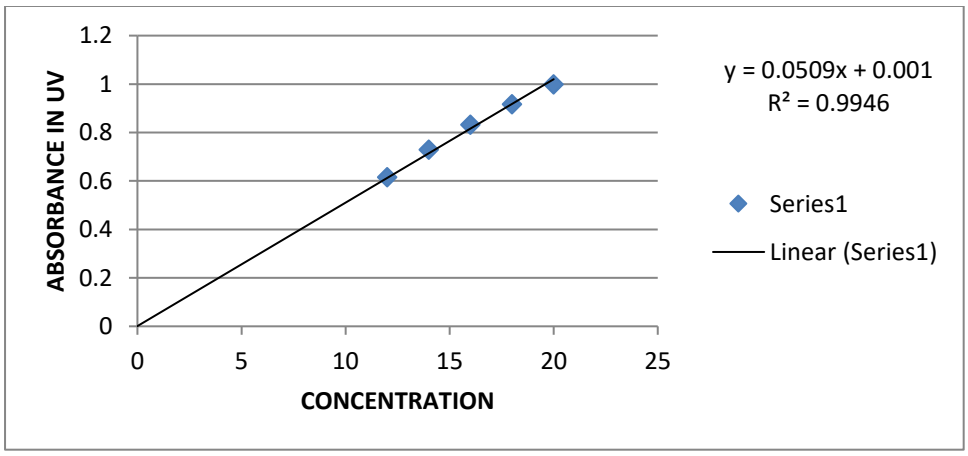

Figure No 5: Standard Calibration Curve of Tacrolimus

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STANDARD CALIBRATION CURVE OF SULPHAMETHOXAZOLE

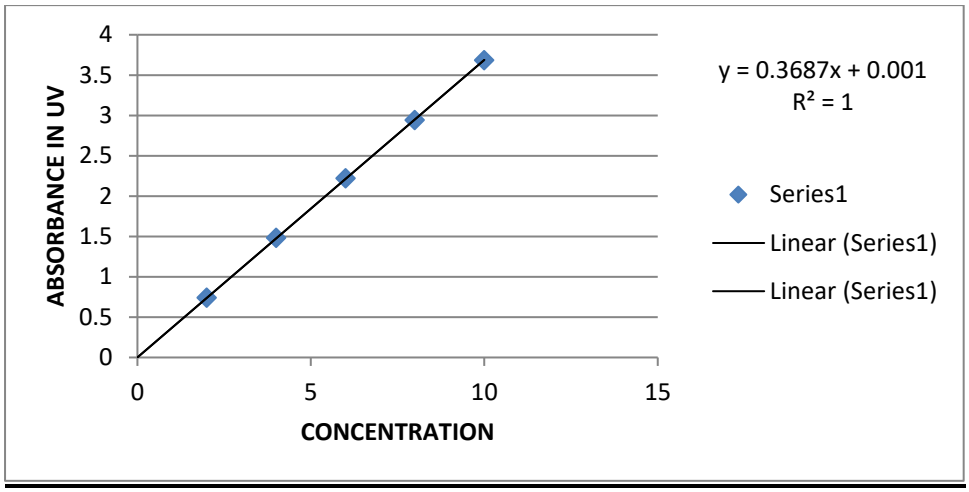

Figure No 6: Standard Calibration Curve of Sulphamethoxazole

STANDARD CALIBRATION CURVE OF TRIMETHOPRIM

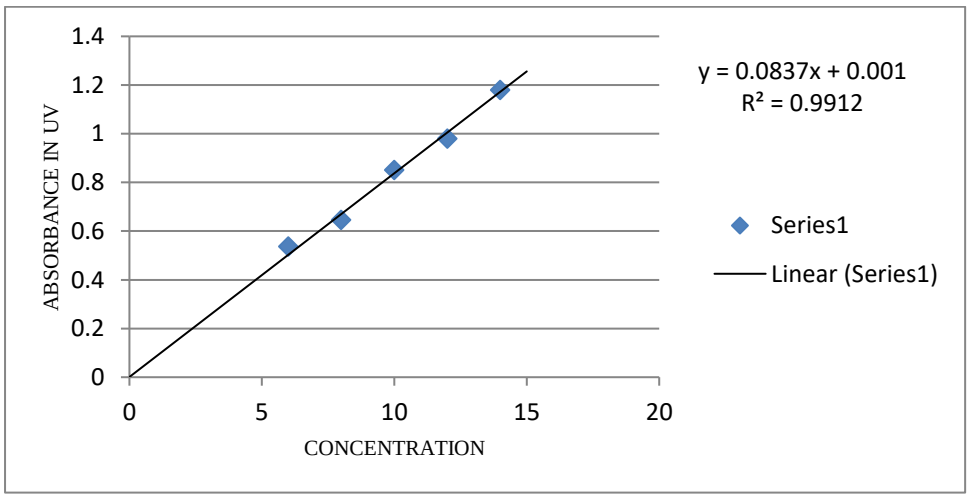

Figure No 7: Standard Calibration Curve of Trimethoprim

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5. Preparation of Sustain Release Tablet by Wet Granulation Method and Formula

Table No. 5: Formulation Of Sustain Release Tablets of Tacrolimus and Cotrimaxazole

Ingredient	Formulation code	F1	F2	F3	G4	G5	G6	H7	H8	H9
Tacrolimus		10	10	10	10	10	10	10	10	10
trimethoprim		160	160	160	160	160	160	160	160	160
Sulphamethoxazole		800	800	800	800	800	800	800	800	800
Eudrogitrspo	F	7.5	10	5	-	-	-	-	-	-
PVP		12.5	10	20	-	-	-	-	-	--
Gum copal	G	-	-	-	5	9.5	6	-	-	-
Bean gum		-	-	-	15	10.5	14	-	-	-
Gum damar	H	-	-	-	-	-	-	9	12.5	6
Guar gum		-	-	-	-	-	-	68.9	56	78
Mg. stearate		4	4	4	4	4	4	4	4	4
Starch I.P		29.75	35	35	29.75	35	35	29.75	35	35
Talcum		4	4	4	4	4	4	4	4	4
Sodium saccharine		4	4	4	4	4	4	4	4	4
Total		1042.1	1037	1042	1031.75	1037	1037	1089.65	1085.5	1101

6. Evaluation of Sustain Release Tablet of Tacrolimus, Sulphamethoxazole and Trimethoprim

Table No.6: Evaluation Of Sustain Release Tablet of Tacrolimus, Sulphamethoxazole and Trimethoprim

Batch	Thickness (mm)	Hardness (kg/cm^2)	Friability (%w/w)	Weight variation
F1	4.36	8.45	0.396	1040
F2	4.42	8.67	0.387	1038
F3	4.40	8.45	0.390	1041
G4	4.54	7.95	0.354	1030
G5	4.55	7.96	0.327	1038
G6	4.57	7.84	0.312	1036
H7	4.61	8.84	0.198	1090
H8	4.59	8.77	0.210	1085

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H9	4.59	8.67	0.234	1100
Marketed tablet of Tacrolimus (Macpod, from Macleods)	5.60	8.78	0.275	1234
Marketed tablet of Sulphamethoxazole(P-125, Apex lab Pvt Ltd.)	4.89	8.24	0.264	1143

6.1 PERCENTAGE DRUG RELEASE OF TACROLIMUS AT 260 NM AND SULPHAMETHOXAZOLE AT 248 NM AND TRIMETHOPRIM AT 237.6 NM

Table No. 7: Percentage Drug Release of Tacrolimus At 260 nm and Sulphamethoxazole At 248 nm and Trimethoprim At 237.6 nm

Sr. no	batches	% drug content for Tacrolimus	% drug content for Sulphamethoxazole	% drug content for Trimethoprim
1	F1	75.6	77.6	76.5 %
2	F2	80.28	66.8	57.6 %
3	F3	90.21	65.97	66.76 %
4	G4	97.38	96.3	90.37 %
5	G5	68.04	68.4	67.14 %
6	G6	74.43	83.5	87.37 %
7	H7	90.27	80.82	81.43 %
8	H8	87.46	78.26	73.64 %
9	H9	88.47	75.8	74.45 %
10	Marketed tablet (indivisually)	92.73	91.97	92.71 %

IN –VITRO DISSOLUTION PLOT OF TACROLIMUS

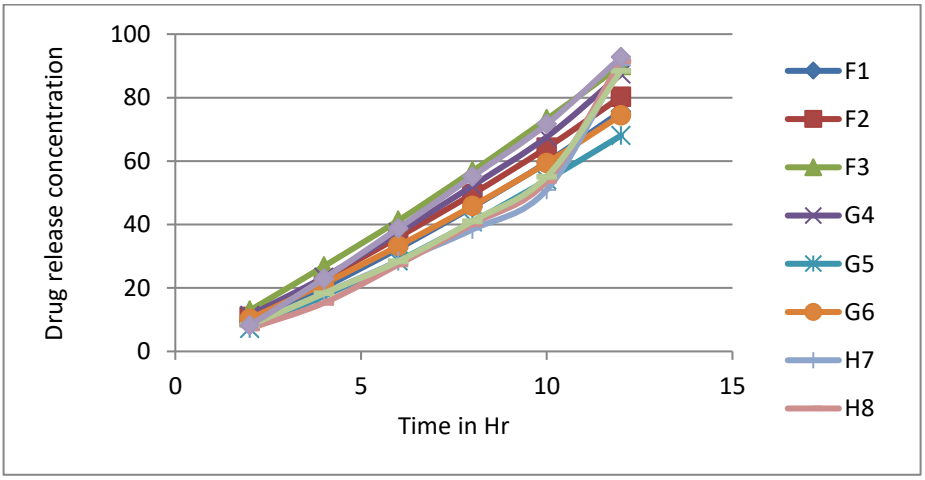

Figure No 8: In –Vitro Dissolution Plot of Tacrolimus

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IN-VITRO DISSOLUTION PLOT OF SULPHAMETHOXAZOLE

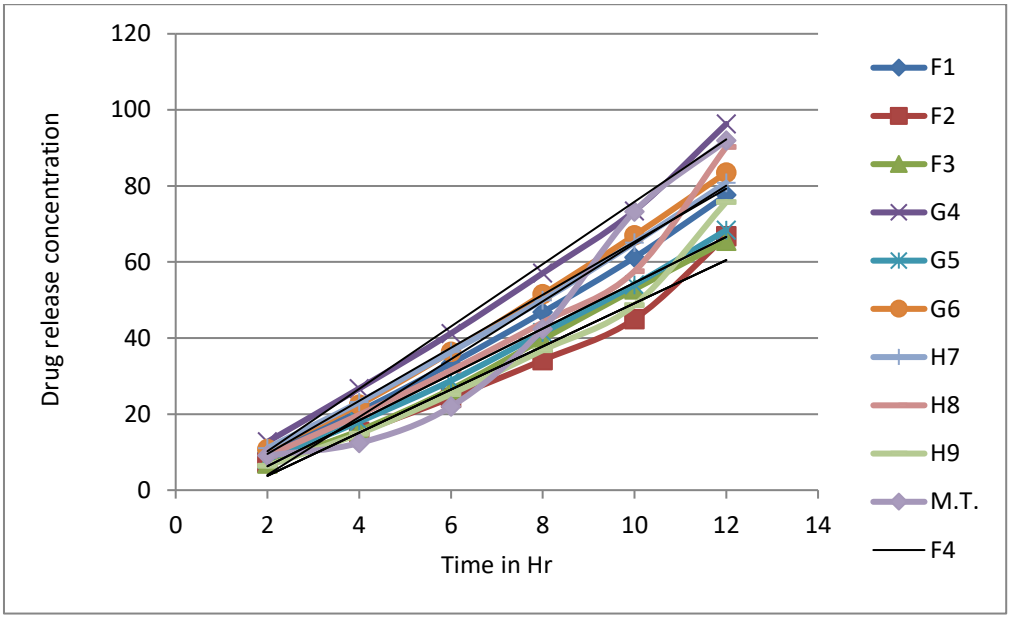

Figure No 9: In-Vitro Dissolution Plot of Sulphamethoxazole

IN-VITRO DISSOLUTION PLOT OF TRIMETHOPRIM

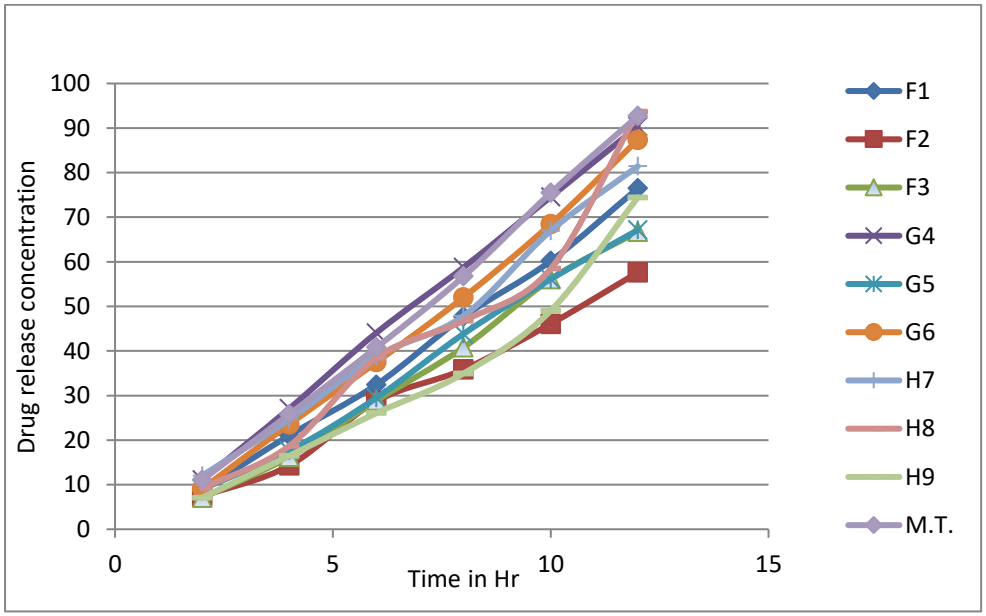

Figure No 10: In-Vitro Dissolution Plot of Trimethoprim

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CONCLUSION

In present study, different polymers were used in combination so that good results can be obtained by prolonging the disintegrate time from 8 – 12 hrs, so that the drug can be absorbed in upper GIT. The batch F4 is found to be best batch producing 97.38% and 96.3%, 90.37 % of Tacrolimus, Sulphamethoxazole and Trimethoprim respectively by giving best time. In addition, it was found that formulation-containing combination of cross-gum copal and bean gum gives a good result as compared to other combination.

There were no incompatibility found between drugs, polymer and excipient. The present study indicates that the oral sustained release tablets of Tacrolimus and co-trimaxazole provides a better option for development of a once-daily formulation of the drug. The analyst was found to be success in combining costly polymer with economical polymer.

SUMMARY

Many pharmaceutical dosages are administered in the form of pills, granules and liquid. Generally, the pills, which include tablet and capsule, are able to retain their shape under moderate pressure. However, some patient, particularly pediatric and geriatric patient, has tendency to miss the solid dosage forms.

One of the primary objectives in developing the sustain release tablet was to identify and satisfy an unmet need of general and specific population and to improve compliance and dosing ease for the patient. This system allows children, elderly and the general population to take their medications discretely wherever and whenever needed, satisfying the need of avoiding multiple dose.

Thus, sustain release drug delivery system are rapidly gaining interest in the pharmaceutical industry. Preparation of sustain release tablet of Tacrolimus and Cotrimaxazole remove the number of intake of tablets. Though tacrolimus is one of the most widely used medicine for organ transplant. It is the drug of choice for all type of organ transplant to inhibit organ rejection. Hence, in the present study it was decided to prepare sustain release tablet for better effect.

The sustain release tablet of Tacrolimus and Cotrimaxazole was prepared by granulation method. Various tests were performed for hardness, friability, disintegration, dissolution. Stability of the sample was determined by HPLC report, which was found to be stable graphically. Whereas drug–drug interaction and drug-polymer are not possible as mechanism of action of all three drug are different from each other.

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