DEVELOPMENT AND EVALUATION OF AEGLE MARMELOS POLYSACCHARIDE AS A MATRIX FORMER

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Abstract:

Background-

Examining the formulation of tablets containing sustained-release metoprolol succinate using Aegle marmelose (Bael), a plant belonging to the Rutaceae family, as the matrix-forming polymer, was the overall objective of the study. Excipients are crucial in improving the quality. Results- Aegle marmelose polymers are used in pharmacy similarly to synthetic polymers, which have numerous potential uses as matrix formers in cutting-edge drug delivery systems. Due to the fact that these polysaccharide gums are abundant naturally, biocompatible, biodegradable, and non-immunogenic, as well as the fact that they contribute to economic growth by allowing people to obtain affordable formulations created with components that are easily accessible locally. They may also be adjusted in a variety of ways to obtain the needed properties of components for drug delivery systems, which puts them on par with the currently accessible synthetic additives. The fruits of the Aegle marmelosto are used as a binder in the preparation of metoprolol succinate matrix tablets. The 3^2 factorial design (F1 to F9) was used to create the metoprolol succinate tablet, and samples from the F6 batch were tested for weight variation, hardness, friability, drug content, drug release research, stability study, solubility study, swelling property, and compatibility with drug excipients. Conclusions- Since there have been no significant changes seen in metoprolol succinate tablets that have been produced and stabilised, aegle marmalose polysaccharide is a more suitable natural binder than synthetic one. Determining the potential of natural polysaccharide was another objective of the study.

Keywords: Aegle marmelose, Metoprlol succinate, Matrix former, Factorial design.

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Introduction:

Due to a few side effects and the toxicity of manufactured pharmaceuticals, products from natural sources have become a significant part of human medical care. Drug stores offer a wide range of supported discharge conditions and use normal polymers similarly to how they use produced polymers. They have an advantage over excipients that are generated commercially and are easily accessible in that they may be tweaked in a variety of ways to create materials that are specifically tailored for drug delivery systems. Diverse polymers have been studied as drug-impeding specialists, and each one offers a different way to manipulate the lattice structure. Given the benefits of the inhibiting polymer for preventing the administration of medication and the usage of hydrophilic polymers, they are the most logical choice.

Use of natural polymers in a drug delivery system for sustained release:

The employment of common polymers and their partially modified variations in the delivery of medications is still being studied. Drug-release-resisting polymers are an essential component of network systems. There are many polymers that have been investigated as potential drug-impeding agents, and each one offers a different approach to treating the framework. According to the properties of the constraining polymer, lattice frameworks are frequently categorised into three major groups: hydrophilic, hydrophobic, and plastic. Using hydrophilic polymers to facilitate drug transport is starting to make money. Hydrophilic polymers are the most effective at inhibiting drug delivery. (4)s Aloe mucilage, fenugreek mucilage, tamarind gum, okra gum, karaya gum, locust bean gum (LBG), guar gum, and honey beetle venom have all been studied as experts in assisted discharge.[1-5]

Plant Description

A medium-sized, aromatic tree, the bale organic product tree is also known as bael (Aegle Marmelos (Linn), family Rutacae. The mash of the mature organic product is crimson in colour and tastes tannic and sticky. The mash is packed with vitamins C and A, proteins, carbs, marmeline, dictamine, angelenine, and other minerals. The acidic and nonpartisan oligosaccharides were represented by the oligosaccharides 3-0-beta-Dgalactopyranosyl-L-arabinose, 5-0-beta-Dgalactopyranosyl-L-arabinose, and 3-0-beta-Dgalactopyranosyl-D-galactose, respectively. Due to their enormous advantages over manufactured polymers, scientists have been using natural biopolymers more frequently in recent years. The best materials are polysaccharide gums since they are abundant in nature, biocompatible, biodegradable, and immune-neutral. [6-8]

Aegle marmelos Gum as Tablet Binder:

The Aegle Marmelose organic product gum was used to hide the oral paracetamol tablet. Wet granulation was used to produce the four various tablet designs. Natural cordia product binder concentrations of 2, 4, 6, and 8% w/w were used for the detailing.

Purification and standardization of Gum- [9-11]

- 250g of the edible fruits from A. marmelos were cooked in a water bath for five hours till slurry formed after being soaked in double-distilled water for one hour.
- In order to ensure that the majority of the undissolved particles settled out, the slurry was chilled and kept in the refrigerator overnight.
- After being decanted off, the upper clear solution was spun for 20 minutes at 500 rpm. At 60^0C on a water bath, the supernatant was concentrated until the volume was just a third of what it had been initially.
- After being brought to room temperature, the solution was added to three times as much acetone while being vigorously stirred.
- The precipitate was regularly rinsed with water and vacuum-dried at 50^0C.

Rationale of sustained release drug delivery

Modifying drug release and developing a dosing pattern that runs quietly regularly is the key principle of assisted drug administration. For addressing chronic sickness, it is the most useful measurement technique. [12--15]

Material and Method:

Metoprolol succinate was obtained from lupin pharmaceuticals. aegle marmalose polymer cellulose was obtained from Charak Ayurveda Jaipur.

Preparation of stock solution

Metoprolol succinate's UV spectrum was measured using the Shimadzu UV1700. To make a stock solution (1000 g/ml), 100 mg of the medicine, carefully weighed, were dissolved in 6.8 phosphate buffer to a volume of 100 ml. By removing 0.1 ml of the aliquot and applying 6.8 phosphate buffer to expand the volume to 10 ml, the concentration was increased to 10 g/ml. After scanning the solution from 200 to 400 nm, the spectra was captured (figure 1).

Preparation of serial dilution

Various aliquots from the stock solution were

gathered and separately diluted with distilled water to create a series of concentrations ranging from 10 to 50 g/ml. Metoprolol succinate's UV spectra were scanned from 200 to 400 nm in a buffer of pH 6.8, and the highest wavelength was discovered to be 223 nm. The absorbance at 223 nm was measured using a UV-Visible Spectrophotometer in comparison to a blank buffer with a pH of 6.8. (UV-1700 SHIMADZU). By plotting the absorbance versus the concentration of metoprolol succinate, the calibration curve was produced.

Drug excipient compatibility study

For the successful creation of a suitable and effective solid dosage form, meticulous excipient selection is paramount. Excipients are added to medications to boost their bioavailability, regular release, and convenience of administration. Excipients' compatibility with medications needs to be investigated. Heat analysis and IR spectroscopy were employed to investigate and predict probable physicochemical interactions between components in a formulation as well as to select compatible excipients.[16]

Physical Compatibility

The physical mixture of the pure medication and polymers in the ratio of 1:1 was used to study the compatibility of the excipients. The mixes were made by triturating the medication with polymers, and they were kept in closed vials at 121°C for 15 minutes. In closed and open vials, at room temperature and 40% relative humidity, for 4 weeks.(table no.10)

Chemical Compatibility-

Differential Scanning Calorimeter (DSC)

Differential scanning calorimetry was used to test drugs and drug-polymer combinations (DSC). Pharmaceuticals and polymers were triturated (1:1) in a dried mortar for 5 minutes to form the physical mixes for compatibility testing. The combinations remained there for the following 24 hours. After being weighed at a range of 2 to 5 mg, the samples were sealed in aluminium pans with the medication and polymer mixture (1:1:1). Over a temperature range, the sealed aluminium pan was heated at a rate of 10°C/min.

Flow determination Drug and Polymer Properties

The calibre of a tablet depends on the calibre of the powder from which it is formed. Therefore, it is vital to evaluate the powder and ascertain whether it complies with the fundamental requirements. In factorial batches, the powder's bulk density, tapped density, Carr's index (compressibility), angle of repose, and Hausner's ratio were all evaluated. The powder's evaluated parameters are reported in the table. Physicochemical properties of aegle marmalose (table no 4)

Loss on drying:

The 5 gm of gum was dried at 105 5 oC until the desired consistency in gum weight was achieved. The drying loss was discovered to be less than 8% w/w.

Ash value:

Accurately weighing 1g of gum, it was then distributed in the crucible in a uniform layer. It was dried for an hour at 105^0 C before being lit in a muffle furnace at 600 ^{0}C and 25^0C. Less than 7% w/w of ash was discovered to be present.(table no 5)

Swelling property of aegle marmalos

Fruits from A. marmelose are not poisonous. Until no further hydration was seen, 250 mg of A. marmelose gum was allowed to hydrate in 25 ml of distilled water at 250C in a 25 ml graduated cylinder, with the volume being measured every five minutes. Various time periods were used to determine the swelling property(table 7)

Stability studies

According to ICH recommendations, the stability analysis of the chosen optimum F6(Tablet) formulations was conducted at accelerated 40^0 C and room temperature, 25°C$\pm$ 2°C/60% $\pm$5% RH%, and room temperature for three months while the samples were kept in a stability chamber (Table 14)

***In vitro* drug release study**

The drug release rate from metopropol succinate SR matrix tablets (n=3) was calculated using USP apparatus type I. (Labindia, India). The dissolving test was conducted using 500 cc of buffer with a pH of 6.8 for 20 hours at 37 $\pm$0.5 C and 50 rpm. A sample (5 ml) was taken out and replaced with fresh dissolving medium at regular intervals in the same volume. The samples were filtered using a Whatman filter paper. A UV-visible spectro-photometer was used to measure the solutions' absorbance at 274 nm (UV-1700 SHIMADZU). The drug release and drug release kinetics were calculated using PCP Disso ver. 3.0. The cumulative drug release of all 9 batches is shown in Tables 11 and the drug release patterns of factorial batches. [17,18,19]

Formulation study

Preliminary trial batches

Table 1 displays the makeup of the initial test batches for the formulation of sustained release. 50 mg of metoprolol succinate was used in each formulation. Wet granulation was employed to create the metoprolol succinate matrix tablets, and the excipients included talc, spray-dried lactose for filler, Aegle marmelos for the matrix, PVP K30 for granulation, and magnesium stearate for lubrication (glidant). The wet granulation method was used to create tablets of the sustained release matrix. All of the materials were carefully weighed, passed through sieve #100, combined, and then granulated with the aid of PVP K-30 in isopropyl alcohol. The resulting granules were dried in an oven for two hours at 50^0C. Granules went through sieve #16 to get a uniform size after drying. [20-21]

Table 1: Composition of preliminary trial batches

Name of Ingredients	P1(mg)	P2(mg)	P3(mg)	P4(mg)	P5(mg)
Metoprolol succinate	**50**	**50**	**50**	**50**	**50**
Spray dried lactose	**181.5**	**179**	**176.5**	**173.5**	**169**
Aegle marmelose	**7.5**	**10**	**12.5**	**15.5**	**20**
PVP K30	**5**	**5**	**5**	**5**	**5**
Mg. stearate	**2**	**2**	**2**	**2**	**2**
Talc	**4**	**4**	**4**	**4**	**4**
Total weight	**250**	**250**	**250**	**250**	**250**

Table 2: Translation of coded values for 3^2 factorial experimental designs

Sr. No.	Coded Value	Level	Experimental Actual Value	
			X1(%)	X2(%)
1	*-1*	*Low*	0.5	2
2	*0*	*Intermediate*	3	5
3	+1	High	5	8

Table 4 displays the makeup of the final optimised batches for the formulation of sustained release. Aegle marmalos and PVP K30 were utilised in concentrations of 2 to 8% and 0.5 to 5%, respectively, as sustained release polymers. In the current investigation, a 32 complete factorial design with 3 components assessed at 2 levels was used, and experimental trials were conducted using all 9 potential combinations. PVP K30(X1) and Aegle marmalos were chosen as the study's independent variables (X2). Table 4 displays the conversion of coded data for 3^2 factorial experimental designs.

Table 3: Formulation of 3^2Factorial Design Batches

Ingredient(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metoprolol succinate	50	50	50	50	50	50	50	50	50
Spray dried lactose	186.5	176.5	179	181.5	174	166.5	169	171.5	161.5
Aegle marmelos	5	5	12.5	5	12.5	20	12.5	20	20
PVP K30	2.5	12.5	2.5	7.5	7.5	7.5	12.5	2.5	12.5
Mg. Stearate	2	2	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4	4	4
Total	250	250	250	250	250	250	250	250	250

Result and Discussion:

Pre compression studies: The pre compression properties of eight formulations (F1 to F8) were studied which includes bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose.

All the results were found to be within limits and indicate the free flow (**table 5)**.

Post compression studies: The post compression properties were performed for all the formulations, which include hardness, friability, thickness, weight variation,in vitro drug release and stability study.

All the formulations were found to be within limits according to IP specifications (**table11**).

The present study was aimed to develop sustain release tablets of Verapamil hydrochloride using various polymers. All the formulations were evaluated for physicochemical properties and in-vitro drug release studies.

UV Spectra

The UV spectrum of Metoprolol succinate solution (50µg/ml) exhibited wavelength of absorbance maximum at 223 nm which complies with the reported.

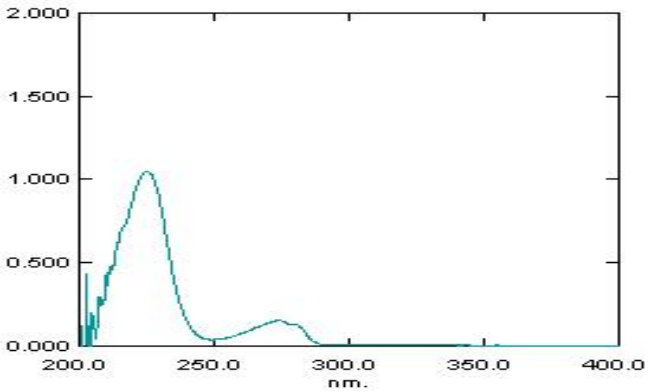

Figure.1 UV spectra of metoprolol succinate

DSC Spectra

DSC thermogram of Metoprolol succinate showed one endothermic peak of fusion,having peak maximum of 139.93°C. This was in accordance with the reported. (Figure 2) On the basis of melting point, UV spectrum, Infrared spectrum and DSC thermogram the procured sample of Metoprolol succinate was found to be of acceptable purity and quality. The sample was taken for further studies.

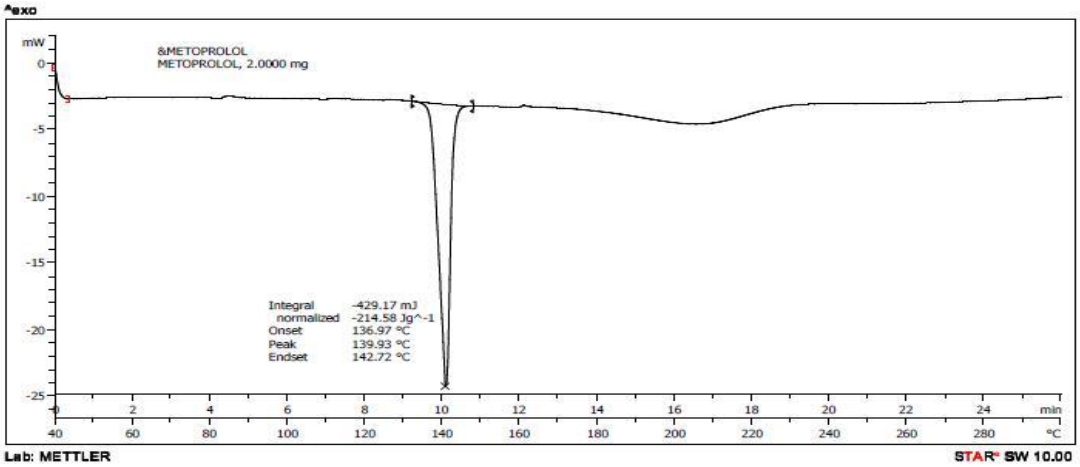

Figure 2: DSC Thermogram of metoprolol succinate

Drug and Polymer flow properties

Table 4. Determination of Flow Properties of Drug and Polymer

Drug/ Polymer	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Carrs Index (%)	Hausner Ratio	Angle of Repose (θ)
Metoprolol succinate	0.475	0.53	11.3209	1.3213	29.79
Aegle marmelos	0.435	0.57	10.96%	1.33	31.12
PVP K30	0.481	0.56	14.31	1.21	27.32.

Table 5: Physicochemical properties of aegle marmelos		
SPECIFIED TEST	**RESULT**	**SPECIFICATION**
Description	Brown coloured dry power	Brown coloured dry power
Solubility in water	72.18%	NLT 70%
Loss on drying	2.02%	NMT 7.0%
Ash value	8% w/w	NLT 7%w/w
pH of 1% solution	4.87	4-7

Table 6:Swelling property of aegle marmelos

Natural gum	After 5 min (ml)	After 10 min (ml)	After 15 min (ml)	After 20 min (ml)	After 30 min (ml)	After 35 min (ml)
Aegle marmalos	0.5	0.7	0.9	1.1	1.3	1.3

Table 7: The solubility of Metoprolol succinate in various medium is shown in following table

Sr. no.	Medium	Solubility(mg/ml)
1.	Water	12.8
2.	0.1 N HCl	21.5
3.	Methanol	99.25
4.	Phosphate buffer pH 6.8	35.5

Analytical method development and validation

The UV spectrophotometric method was selected for estimation of Metoprolol succinate. The UV spectrum exhibited maximum absorbance (λmax) at 223nm. The standard calibration curve exhibited good coefficient of correlation as shown in Table 8

Table 8: calibration curve in phosphate buffer 6.8

CONC(µg/ml)	ABSORBANCE
5	0.134
10	0.258
15	0.366
20	0.479
25	0.604

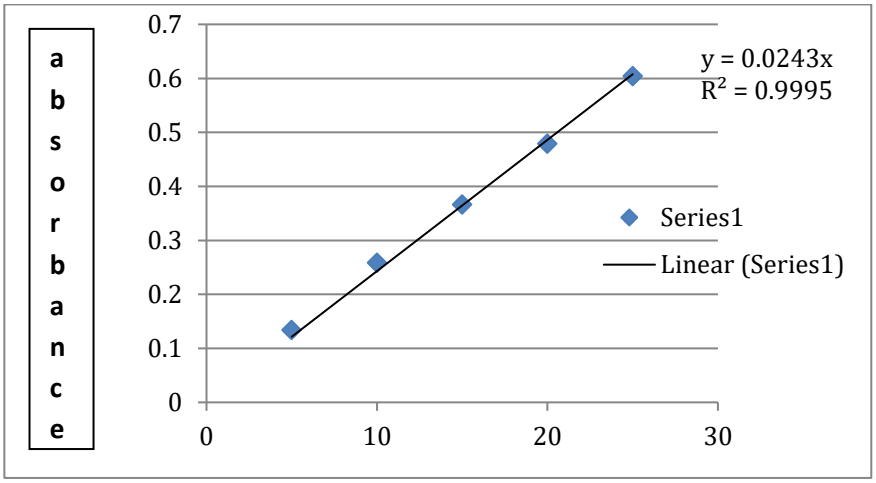

Figure 3:Calibration curve of metoprolol succinate in 6.8 phosphate buffer Analytical method validation

Developed method was validated and validation parameters are listed in Table 9

Table 9: Validation Parameter

Parameter	Limit	Results
Accuracy	98 - 102	99.03
Repeatability	%RSD < 2	0.0881%
Intraday precision	%RSD < 2	1.13561
Inter day precision	%RSD < 2	1.1551
Linearity	R2 > 0.9997	0.999
Range	%RSD < 2	5-25((µg/ml)
LOD	-	0.7671((µg/ml)
LOQ	-	2.3248((µg/ml)

Drug excipients compatibility

Physical Compatibility

In all physical mixtures of drug and polymer, there was no physical change observed.

Table 10: Shows Excipient Compatibility Study

Sr No	Conditions	Time	Open\Closed	Observations
1	121º C	15 min	closed	No Colour change
2	Room temp	4 weeks	closed\ open	No Colour change
3	Refrigerator	4 weeks	Closed\ open	No Colour change
4	40º C/75%RH	4 weeks	open No	No Colour change

Chemical compatibility

DSC Studies

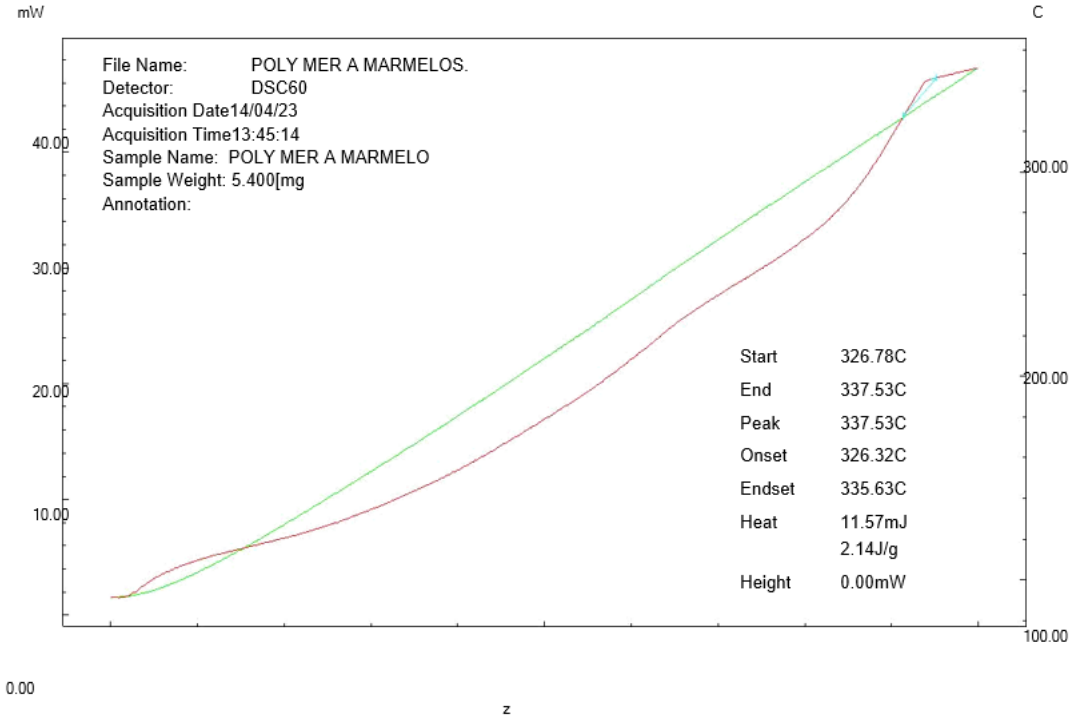

Figure 4. DSC Thermogram of Physical Mixture of aegle marmelos

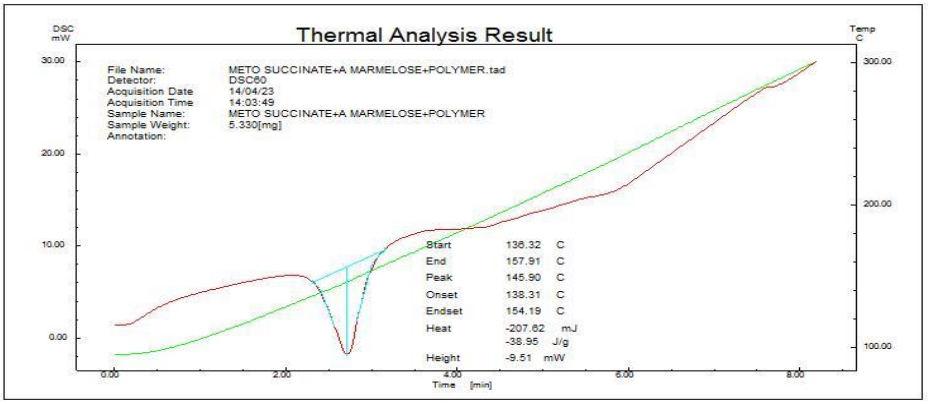

Figure 5:DSC Thermogram of Physical Mixture of metoprolol succinate + aegle marmalos

The endothermic peak at 145.90ºC can be attributed as melting point of Metoprolol succinate. The thermogram showed that the Metoprolol succinate and aegle marmelos compatible with each other(fig.5)

FORMULATION STUDIES

Preliminary Trial Batches

Results showed that the drug release increases with increase in the concentration of aegle marmalos gum.

DISSOLUTION PROFILE

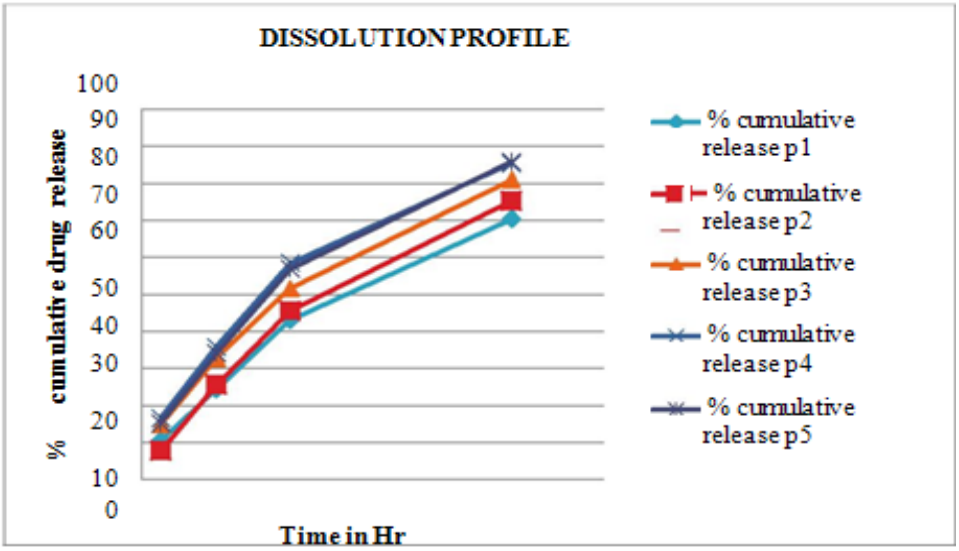

Figure 6: % cumulative drug release of primary batches

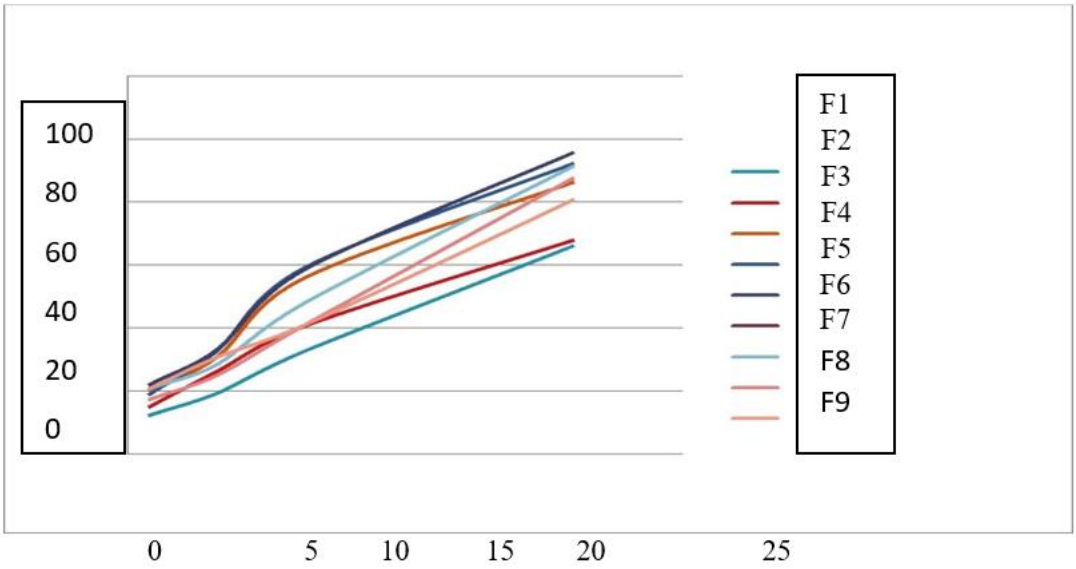

Figure 7: % cumulative drug release of final batch

Table 11: Evaluation parameters of final batches

Batch	Appearance	Weight variation mg ± SD	Hardness (Kg/cm^2) ±SD	Friability%	Thickness (mm) ±SD	% Drug release
F1	Brownish	249±0.47	6.3±0.28	0.61±0.02	3.18±0.12	65.94%
F2	brownish	250±0.81	6.1±0.5	0.71±0.04	3.20±0.220	67.84%
F3	brownish	250±1.69	6.7±0.31	0.65±0.09	3.18±0.03	86.24%
F4	brownish	250±1.24	6.3±0.21	0.52±0.03	3.20±0.13	71.2%
F5	brownish	250±0.47	6.6±0.28	0.60±0.06	3.24±0.11	92.15%
F6	**brownish**	**250±0.71**	**6.7±0.31**	**0.52±0.03**	**3.18±0.03**	**95.63%**
F7	brownish	250±0.47	6.3±0.31	0.65±0.09	3.20±0.220	91.33%
F8	brownish	250±0.48	6.7±0.28	0.61±0.02	3.18±0.03	87.39%
F9	brownish	250±0.47	6.8±0.28	0.65±0.09	3.20±0.220	80.58%

Drug release kinetic studies of tablet formulation

Formulation F6 shows significant good release for 20 hrs with low burst effect. The formulation having concentration 20mg of aegle marmelos and 7.5mg PVPk30 exhibited the extended cumulative percentage of drug release value (95.633%) after 20 hr of gum. The drug release follows the Higuchi release pattern i.e. diffusion followed by erosion.

Table 13: Drug release kinetic studies of tablet formulation

Formulations	Zero order kinetics	First order kinetics	Higuchi square root equation	Regression coefficient
F6	0.9231	0.9145	0.9990	0.5176

STABILITY STUDY-

Table 14: Physico-Chemical Evaluation Of Selected Matrix Tablets Before And After Stability Study

ICH conditions	Hardness test (kg/cm2)		% Drug Release	
	Before	After	Before	After
45 ±2°C/75 ± 5% RH	6.7±0.31	6.9±0.31	95.6334%	90.23%
Room Temp.	6.7±0.31	6.8±0.24	95.633%	92.45%

CONCLUSION

Modern medicine administration systems frequently employ the oral modified discharge dose formulations. Reducing medication dosage repetition and total dose with the SR lattice framework lowers the medication's side effects. One of the drugs that the network SR structure distributes throughout the G.I. parcel is metoprolol succinate, which reaches its maximal medicine release level quickly before progressively slowing down over time. Regular biopolymers should be used instead of synthetic polymers because of their extensive benefits. The initial clusters of details were completed and evaluated; out of five groups, group P5 demonstrated the release of medication in accordance with USP. This shows that using aegle marmelose 20 mg is the optimal convergence. F6 is the optimal plan, according to future research employing a 32 factorial plan, to demonstrate the most intense pharmaceutical release. The results of the current review reveal that conventional gums were regarded as useful in identifying the assisted delivery lattice tablets of metoprolol. It became clear that the 20 mg gums' centralization was suitable for delaying the arrival of medication for 20 hours and successful in creating the sustained-release matrix tablets of metoprolol..

REFERENCES

[1]. Khan GM.(2001) Review, Controlled release oral dosage forms: some recent advances in matrix type drug delivery systems. The Sciences 2001; 1(5): 350-354. 2.

[2]. Indian Pharmacopoeia: Ministry of Health and Family Welfare, Govt. of India, Controller of Publications, New Delhi 1996:Vol.II, A100 - A111.

[3]. Kulkarni GT, Suresh B(2002) Evaluation of binding properties of plantago ovate and trigonellagaecum mucilages. Indian Drugs. 2002; 39 (8): 422-425 .

[4]. Evans WC, Trease and Evans. Pharmacognosy. Harcourt Brace & Co., Asia Pvt. Ltd, Singapore.14th Edition (1996); 196, 208, 209, 213-215, 462, 555

[5]. Jagetia GC, Venkatesh P. Radioprotection by oral administration of *Aegle marmelos* (L.)Correa *in-vivo*. *J Environ Pathol Toxicol* (2005); 24: 315-32.

[6]. C.S.I.R.(1985), " The wealth of India" National Institute of Science communication and Information Resources", Volume- I (A), 86.

[7]. Purohit S. S and Vyas S. P, "In: Aeglemarmelos Correa ex Roxb,(Bael), Medicinal plant c Jagetia GC, Venkatesh P. Radioprotection by oral administration of *Aegle marmelos* (L.)

[8]. Correa *in-vivo*. *J Environ Pathol Toxicol* (2005); 24: 315-32.ultivation- A scientific approach", Agrobios, Jodhpur, 2004. P.P.498-504

[9]. Ritger PL, Peppas NA: A simple equation for description of solute release II Fickian and anomalous from swellable devices. J. Control. Rel. 1987: 5: 37-42.

[10]. Jagetia GC, Venkatesh P. (2005) Radioprotection by oral administration of *Aegle marmelos* (L.) Correa *in-vivo*. *J Environ Pathol Toxicol* 2005; 24: 315-32.

[11]. Badam L, Bedekar SS, Sonawane KB, Joshi SP: *In vitro* antiviral activity of bael (*Aegle marmelos* Corr.) upon human coxsackieviruses B1-B6. *J Commun Dis* 2002; 342: 88-99.

[12]. Acharya G., Kinam P., Mechanisms of controlled drug release from drug-eluting stents, *Advanced Drug Delivery Reviews***,** 2006, 58, pp 387 – 401.

[13]. Modi S. A., Sustained release drug delivery system : A review, *ijprd*, 2011, 2(12), pp 147-160.

[14]. Costa, P.; Lobo, J. M. S. Modeling and Comparison of Dissolution Profiles, *Euro.J.Pharm.Sci*, 2001, 12, pp 123-133.

[15]. Clarke"s. *Analysis of Drugs and Poisions*, Pharmaceutical Press: London (UK), Part II-5,3rd edition, 2004, pp 809-810

[16]. Wells, J. Pharmaceutical preformulation. *Pharmaceutics: The Science of Dosage Form Design.* M. E. Aulton., Eds.; 3rd, Edinburgh London: Melbourne and New York, 1988, p 224, 235-236, 247-250

[17]. Code Q2A, Text on Validation of Analytical

Procedures. Consensus Guideline, ICH Harmonised Tripartite Guidelines, 1994, pp 1-5. 44 Code Q2B, Validation of Analytical Procedures: Methodology. ICH Harmonised Tripartite Guidelines. Geneva, Switzerland: 1996, pp 1-8.

[18]. Code Q2B, Validation of Analytical Procedures: Methodology. ICH Harmonised Tripartite Guidelines. Geneva, Switzerland: 1996, pp 1-8.

[19]. Chien YW, Swarbrick J, Balyan JC. Encyclopedia of Pharmaceutical Technology. New York: CRS press; 1990

[20]. Ratial DA, Gaikwad PD, Bankar VH, Pawar SP. A review on sustained released technology. Int J Res Ayur and Phar 2011; 2(6): 1701-1708.

[21]. Ray Brijesh, Gupta MM. Formulation and evaluation of once daily sustained release matrix tablet of verapamil hydrochloride. Journal of Drug Delivery & Therapeutics 2013; 3(1): 55-58