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Spectrophotometric Estimation of Valacyclovir by Zero Order and First Order Derivative Method in Bulk and Tablet Dosage Form

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Abstract

A rapid, specific and economic two UV-spectrophotometric methods have been developed using two different solvents of 0.1N NaOH and a hydrotropic solution of 1M urea to determine the valacyclovir content in bulk and tablet dosage forms. The valacyclovir was dissolved and prepared in appropriate concentration of 20µg/ml in two different solvents and scanned in the range of 400 to 200 nm and the λmax was noted. The two zero order λmax are 265 nm for 0.1N NaOH and 255 nm for 1M hydrotropic solution (urea) where as 280 nm for 1st order Derivative for 0.1N NaOH. Both the solutions proved linear in the range of 5-25 µg/ml in 0.1N NaOH (0^0 order Derivative) and 5-25 µg/ml in 1M urea (0^0 order Derivative) solution with a good correlation coefficient of r^2=0.9991 and r^2=0.9984 and excellent mean recovery for both the methods were 100.60 % and 101.4333% where as linear in the range of 5-25 µg/ml in 0.1N NaOH for (1st order Derivative) solution with a good correlation coefficient of r^2=0.9991 with excellent mean recovery for both the methods were 100.70%. All these methods were successfully applied for the determination of valacyclovir content in one marketed brand of India and the results obtained were too good with the label claims. The methods were validated statistically and by recovery studies for linearity, precision, repeatability, and reproducibility. The obtained results proved that the methods can be employed for routine analysis of valacyclovir in bulk as well as in the commercial tablet formulations. The method was validated as per ICH guidelines.

Keywords: Valacyclovir, UV-spectrophotometric, λmax, absorption maxima, validation & ICH

Introduction

Valacyclovir is chemically 2-[(2-amino-6-oxo-6,9-dihydro-3H-purin-9-yl)methoxy]ethyl (2S)-2 amino-3-methylbutanoate[1-3]. Valaciclovir (INN) or Valacyclovir (USAN) is a prodrug and synthetic purine nucleoside analogue with inhibitory activity against herpes simplex virus types 1 (HSV-1), 2 (HSV-2), varicella-zoster virus (VZV), Epstein-Barr virus (EBV), and cytomegalovirus (CMV). Valaciclovir is almost completely converted to acyclovir and L-valine [4-6]. The inhibitory activity of valaciclovir is highly selective due to its affinity for the enzyme thymidine kinase (TK) encoded by HSV and VZV. This viral enzyme converts acyclovir into acyclovir monophosphate, which is then converted into acyclovir diphosphate and triphosphate by cellular enzymes. Acyclovir is selectively converted to the active triphosphate form by cells infected with herpes viruses. Valaciclovir is

phosphorylated by viral thymidine kinase to acyclovir triphosphate (the active metabolite) which then inhibits herpes viral DNA replication by competitive inhibition of viral DNA polymerase, and by incorporation into and termination of the growing viral DNA chain [7]. When used as a substrate for viral DNA polymerase, acyclovir triphosphate competitively inhibits dATP leading to the formation of faulty DNA [7]. This is where acyclovir triphosphate is incorporated into the DNA strand replacing many of the adenosine bases. It results in the prevention of DNA synthesis, as phosphodiester bridges can longer to be built, destabilizing the strand [8,9]. In previous studies, only one assay has been reported for the simultaneous determination of valacyclovir and acyclovir in human serum and urine by UV detection[10]. Recently, the chemical and enzymatic stability of valacyclovir has been investigated by HPLC with UV detection[11]. Valacyclovir has also been quantified in pharmaceutical preparations, human serum and biological fluids by HPLC with UV detection and enantioselective HPLC with UV detection[12-14]. Although the ultraviolet spectrophotometric methods are the instrumental methods of choice commonly used in industrial laboratories because of their simplicity, selectivity, and sensitivity. As of our knowledge no report has been mentioned in the literature for the determination of valacyclovir by UV method. The aim of the present work was to develop simple, rapid, accurate, and sensitive UV spectrophotometric method for the determination of valacyclovir in pure and pharmaceutical formulation. According to ICH Guidelines[15], a degradation product is an impurity resulting from a chemical change in the drug substance brought about during manufacture and/or storage of the new drug product by the effect of for example, light, temperature, pH, water or by reaction with an excipient and/or the immediate container closure system.

Materials and methods

Chemicals: The reagents Methanol, Acetic acid, NaOH and HCl were procured from SD Fine Chemicals (AR grade), India. Valacyclovir tablets were procured from Cipla. Double distilled water was prepared in the laboratory. Other chemicals were purchased from local market.

Equipments: The instruments used for the study was Electronic balance (sigma200), Sonicator (PCi-3.5L) and UV spectrophotometer (Shimadzu UV-1800, Japan).

Methods

Solubility Test: Solubility test for the drug Valacyclovir was performed by using various solvents. The solvents include water, 0.1N NaOH, 1M urea in water as hydrotropic solvent, methanol, ethanol, acetonitrile and chloroform.

Determination of λmax:

Preparation of Stock Solution: Standard stock solution of Valacyclovir was prepared by dissolving 10mg of Valacyclovir in 10ml of 0.1N NaOH and 1M urea which gives a concentration of 1000 µg/ml. One ml of this stock solution was taken and was diluted up to 10 ml by using 0.1N NaOH and 1M urea (as solvent) to produce a concentration of 100 µg/ml solution.

Preparation of Working Solution: From the above stock solution 1.5 ml was transferred into 10

ml volumetric flask and volume was made up to the mark with 0.1N NaOH and 1M urea (solvent) to make a concentration of 15µg/ml. Then the sample was scanned with UV-Vis Spectrophotometer in the range of 400-200 nm against 0.1N NaOH & 1M urea as blank and the wavelength corresponding to maximum absorbance was noted at 265nm and 280nm for zero order and first order derivative for 0.1N NaOH and 255nm for 1M urea in doubled distilled water as a hydrotropic mixture.

Preparation of Calibration Curve: From the above stock solution (100 µg/ml) appropriate dilution were made and the volume was made up to 10ml with 0.1N NaOH and 1M urea solution in water to produce the following concentrations of 5 µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml and 25 µg/ml respectively. Then the calibration curve was constructed and found to be straight line [Figure 4 (a) and (b)]. The correlation coefficient was found to be 0.9991 and 0.9934 for zero order and first order derivative for 0.1N NaOH solution respectively and 0.9984 for 1M urea in water [Figure 4(c)]

Method validation

Validation is a process of establishing documented evidence, which provides a high degree of assurance that a specific activity will consistently produce a desired result or product meeting its predetermined specifications and quality characteristics[8].

The validation for UV method development was performed using parameters like Linearity, Accuracy, Precision, Robustness, Ruggedness, Limit of detection (LOD) and Limit of quantification (LOQ)[8].

Linearity: Five separate series of solutions of Valacyclovir, 5-25µg/ml were prepared from the stock solution and analyzed (Table 1 & 2).

Accuracy: Recovery study was performed at 80%, 100% and 120% levels in triplicate. The recovery results showed that the proposed method has an acceptable level of accuracy for Valacyclovir which is from 80% - 120% of test concentration was found from 98.88-102.75% (Table 1 & 3)

Precision: Precision of the method was demonstrated by intraday and interday variation studies. In intraday variation study of 6 different solutions of same concentration of 4µg/ml were analyzed three times in a day and the absorbance was noted. From the absorbance result mean, standard deviation and %RSD was calculated (Table 4).

In the interday variation studies, solution of same concentration of 4µg/ml were analyzed three times for the three consecutive days and from the absorbance result mean, standard deviation and %RSD was calculated and given in (Table 6).

Specificity: 100mg of Valacyclovir was spiked with 50% (50mg), 100% (100mg), and 150% (150mg) of excipient (talc) and the sample was analyzed for % recovery of Valacyclovir (Table 5).

Robustness: Robustness of the method was determined by carrying out the analysis under different temperature conditions i.e. at room temperature and at 18 °C. The respective absorbances of 4µg/ml were noted and the result was indicated as % RSD (Table 8).

Ruggedness: Ruggedness of the method was determined by carrying out the analysis by different analyst and the respective absorbance of 4µg/ml was noted. The result was indicated as % RSD (Table no.8).

Limit of Detection (LOD): LOD was determined by preparing solutions of lower concentrations from Linearity range (2µg/ml). (Table no. 9). Equation is shown below[9].

$$LOD = 3.3 \times S.D / Slope$$

The LOD for Valacyclovir by zero order in 0.1N NaOH was found to be 0.01µg/ml.
The LOD for Valacyclovir by 1st order Derivative in 0.1N NaOH was found to be 0.01µg/ml.
The LOD for Valacyclovir by zero order in 1M Urea was found to be 0.02µg/ml.

Limit of Quantification (LOQ): The LOQ was calculated using the formula involving standard deviation of response and slope of calibration curve (Table no.9). Equation is shown below[9]

$$LOQ = 10 \times S.D / Slope$$

The LOD for Valacyclovir by zero order in 0.1N NaOH was found to be 0.003µg/ml.
The LOD for Valacyclovir by 1st order Derivative in 0.1N NaOH was found to be 0.003µg/ml.
The LOD for Valacyclovir by zero order in 1M Urea was found to be 0.006µg/ml.

Assay of Valacyclovir Tablets (Valacyclovir - 500mg)

A quantity of powder equivalent to 100 mg of Valacyclovir was taken in a 100ml volumetric flask and it was dissolved and diluted up to the mark with the 0.1N NaOH & 1M Urea. The resultant solution was ultra-sonicated for 10 minutes. The solution was then filtered using Whatmann filter paper No.40. From the filtrate, appropriate dilutions were made in 0.1N NaOH & 1M Urea to obtain the desired concentration (4µg/ml). This solution was then analyzed in UV and the result was indicated by % purity given in Table 7.

Results

Validation

Table 1: Linearity

Sl. No.	Conc. (µg/ml)	0° order Derivative Abs Using 0.1N NaOH (265nm)	1st order Derivative Abs Using 0.1N NaOH (280nm)	0° order Derivative Abs Using 1M Urea (255nm)
1	0	0	0	0
2	5	0.138	0.007	0.225
3	10	0.335	0.020	0.510
4	15	0.520	0.029	0.821
5	20	0.695	0.038	1.130
6	25	0.865	0.046	1.373

Table 2: Optical characteristics

Optical characteristics	0^0 order Derivative Abs Using 0.1N NaOH (265nm)	1st order Derivative Abs Using 0.1N NaOH (280nm)	0^0 order Derivative Abs Using 1M Urea (255nm)
Beer's law limit (µg/ml)	5-25 µg/ml	5-25 µg/ml	5-25 µg/ml
Molar extinction coefficient (1 mole-1cm1)	$1.689x10^4$	$0.674x10^4$	$1.654x10^4$
Correlation coefficient	0.9991	0.9934	0.9984
Regression equation (y*)	Y=0.0363x-0.0329	Y=0.0019x-0.0004	Y=0.0584x-0.0632
Slope (a)	0.0363	0.0019	0.0584
Intercept (m)	-0.0329	-0.0004	-0.0632

Table 3: Accuracy

No.of Preparations	Conc. (µg/ml)		0^0 order Derivative Abs Using 0.1N NaOH (265nm)		1st order Derivative Abs Using 0.1N NaOH (280nm)		0^0 order Derivative Abs Using 1M Urea (255nm)	
	Formulation (µg/ml)	Pure Drug (µg/ml)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)
80%	10	8	98.2	1.138	101.2	0.981	102.8	1.626
100%	10	10	102.1	12	101.7	640	101.9	9
120%	10	12	101.5		99.2		99.6	

Table 4: Precision: Repeatability

Conc. (µg/ml)	0^0 order Derivative Abs Using 0.1N NaOH (265nm)	1^{st} order Derivative Abs Using 0.1N NaOH (280nm)	0^0 order Derivative Abs Using 1M Urea (255nm)	0^0 order Derivative Abs Using 0.1N NaOH Statistical analysis	1^{st} order Derivative Abs Using 0.1N NaOH Statistical analysis	0^0 order Derivative Abs Using 1M Urea Statistical analysis
15	0.513	0.0290	0.825	Mean=0.527	Mean=0.0293	Mean=0.823
15	0.519	0.0295	0.823	SD=0.005278	SD=0.000350	SD=0.003386
15	0.521	0.0293	0.822	%RSD=1.011	%RSD=1.194	%RSD=0.411
15	0.528	0.0295	0.829			
15	0.525	0.0289	0.819			
15	0.524	0.0296	0.822			

Table 5: Specificity

Sl. No.	Excipient Conc.%)	Valac-yclovir Input (mg)	0^0 order Derivative Abs Using 0.1N NaOH (265nm)			1st oder Derivative Abs Using 0.1N NaOH (280nm)			0^0 order Derivative Abs Using 1M Urea(255nm)		
			Rec. (mg)	S.D	RSD %	Rec. (mg)	S.D.	RSD %	Rec. (mg)	S.D.	RSD %
1.	50	10	10.43	0.102	0.990	10.78	0.0720	0.67	10.00	0.01	0.1362
2.	100	10	10.27	144	41	10.789	21	03	10.02	365	5
3.	150	10	10.24			10.66		99	10.03		

Table 6: Intra-Inter assay Precision

Precision	Sample No.	Conc. (µg/ml)	0^0order Derivative Abs Using 0.1N NaOH (265nm)		1st order Derivative Abs Using 0.1N NaOH (280nm)		0^0 order Derivative Abs Using 1M Urea (255nm)	
			S.D	%RSD	S.D	%RSD	S.D	%RSD
Intra Day	1.	5	0.00152	1.114	0.000115	1.88	0.001	0.435
	2.	15	0.00378	0.719	0.000152	0.574	0.00305	0.317
	3.	25	0.00378	0.436	0.00023	0.502	0.00208	0.153
Inter Day	1.	5	0.00115	0.88	0.0001	1.59	0.00305	1.35
	2.	15	0.00305	0.557	0.000208	0.715	0.00351	0.430
	3.	25	0.00208	0.242	0.000305	0.673	0.00416	0.307

Table 7: Analysis of Valacyclovir (assay) by proposed method

Tablet- Valacyclovir , Company Name- Cipla ,	Valcivir (500mg)		
Method	0.1N NaOH 0^{o} order derivative	0.1N NaOH 1^{st} order derivative	1M Urea 0^{o} order derivative
Labeled claim (mg)	500.00	500.00	500.00
Amount found (mg)	492.00	496.30	489.80
% Label claim	98.40	99.26	99.76

Table 8: Test for Robustness & Ruggedness

Method	**Condition**	**Conc. (µg/ml)**	**0^{0}order Derivative Abs Using 0.1N NaOH (265nm)**		**1^{st} order Derivative Abs Using 0.1N NaOH (280nm)**		**0^{0}order Derivative Abs Using 1M Urea(255nm)**	
			SD	**%RSD**	**SD**	**%RSD**	**SD**	**%RSD**
Robustness	Analyst-1	15	0.00721	1.37	0.000282	0.978	0.00283	0.34
	Analyst-2	15	0.00378	0.719	0.000152	0.574	0.00305	0.317
Ruggedness	Room Temp	15	0.0041	0.792	0.000282	0.978	0.00777	0.978
	Temp. $18^{O}C$	15	0.00305	0.557	0.000208	0.715	0.00351	0.430

Table 9: Summary of Validation:

Parameter	**0^{0}order Derivative Abs Using 0.1N NaOH(265nm)**	**1^{st} order Derivative Abs Using 0.1N NaOH(280nm)**	**0^{0} order Derivative Abs Using 1M Urea(255nm)**
Range	5-25 µg/ml	5-25 µg/ml	5-25 µg/ml
Linear regression equation	0.0363X-0.0329	0.001X-0.000	0.0584X-0.0632
Linearity indicated by correlation coefficient	0.9991	0.9934	0.9984
Precision indicated by %RSD	0.708429	1.018285	0.486143
Limit of Detection	0.01	0.01	0.02
Limit of Quantification	0.003	0.003	0.006
Robustness & Ruggedness indicated by %RSD	0.8595	0.81125	0.51625

Parameter	0^0order Derivative Abs Using 0.1N NaOH(265nm)	1^{st} order Derivative Abs Using 0.1N NaOH(280nm)	0^0 order Derivative Abs Using 1M Urea(255nm)
Accuracy indicated by % recovery	102.9667	106.0333	101.4333
Specificity indicated by % recovery	103.1333	107.43	100.176
Assay%	98.4	99.26	99.76

Figures

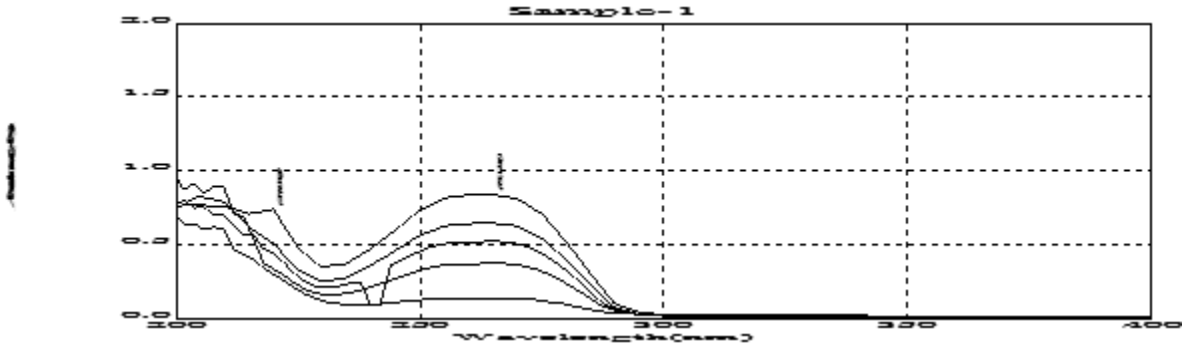

Figure 1: λmax of Valacyclovir at 265nm using 0.1N NaOH (5-25µg/ml)

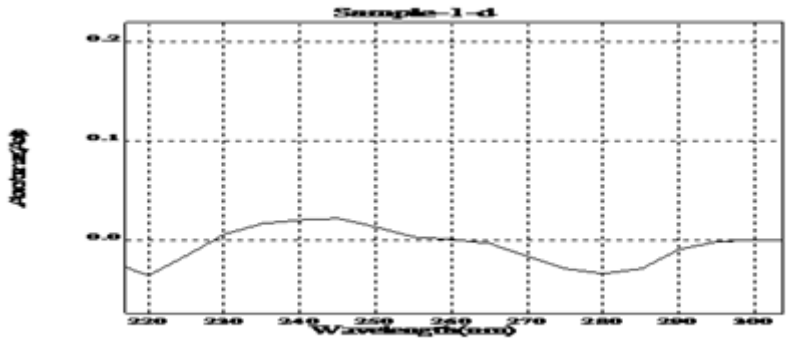

Figure 2: λmax of Valacyclovir at 280nm using 0.1N NaOH in 1^{st} order Derivative (5-25µg/ml)

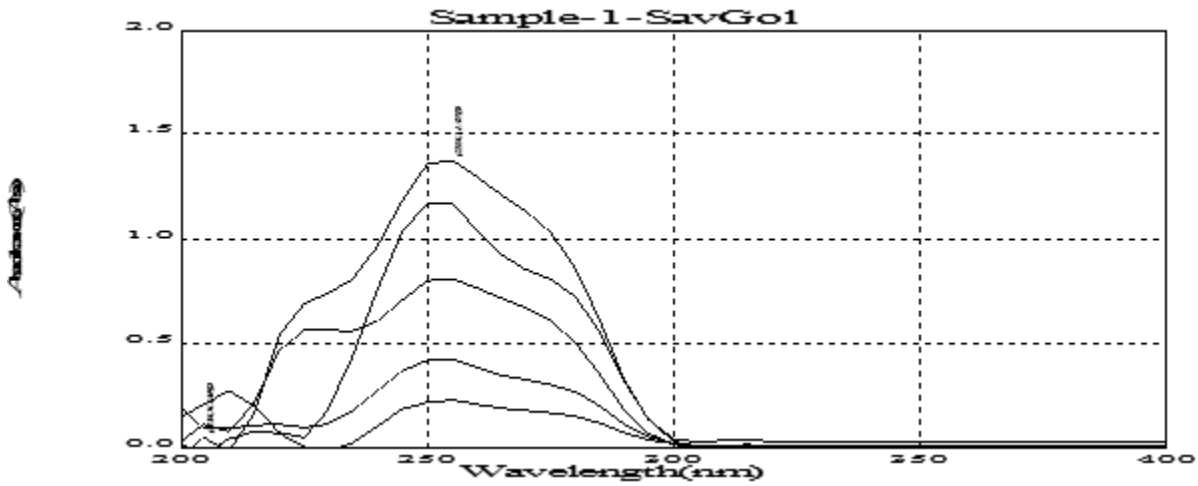

Figure 3: λmax of Valacyclovir at 255nm using 1M Urea in water as a solvent (5-25µg/ml)

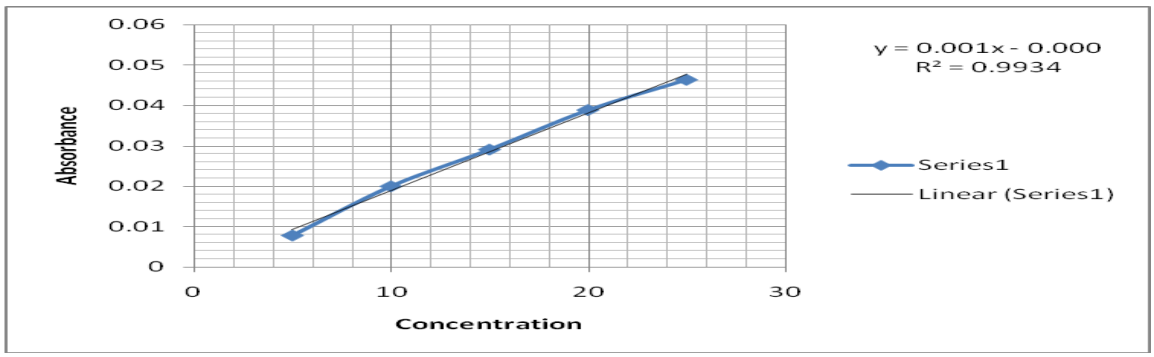

Figure 4(a): Calibration curve of Valacyclovir using 0.1N NaOH at 265nm (0^0 Derivative).

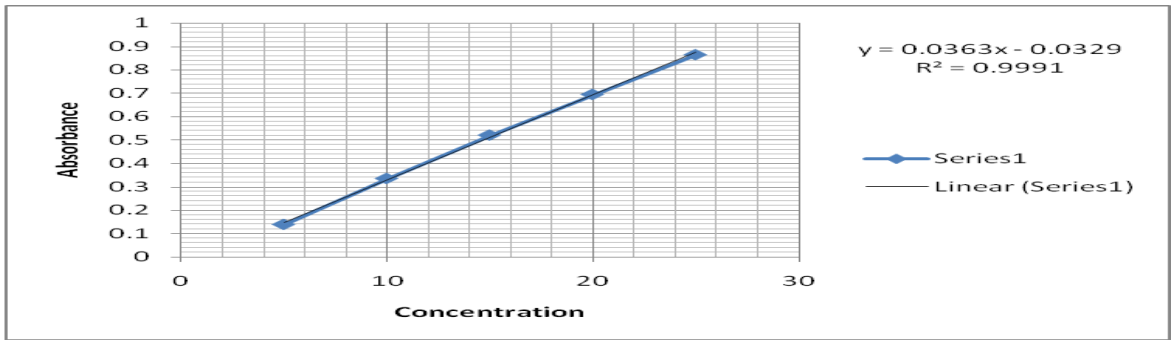

Figure 4(b): Calibration curve of Valacyclovir using 0.1N NaOH at 280nm (1^{st} order Derivative).

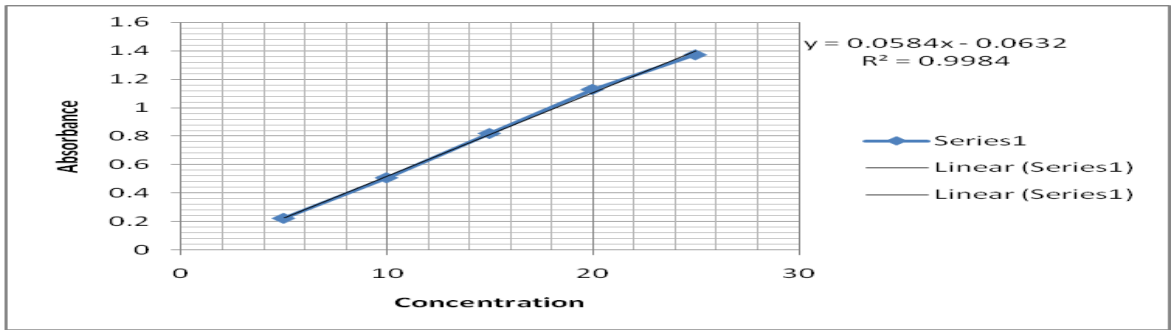

Figure 4(c): Calibration curve of Valacyclovir using urea at 255nm (0^0 Derivative).

Conclusion

The developed method was found to be precise as the %RSD values for intra-day and inter-day were found to be less than 2%. Good recoveries (98.88-100.25% & 101.13-102.75% for zero order and 1st order Derivative order derivative respectively) of the drug were obtained at each added concentration, indicating that the method was accurate. The method was also found to be specific indicated by the % recoveries ranging from 98.88% to 102.75%. The LOD and LOQ were found to be in sub-microgram level indicating the sensitivity of the method. The method was also found to be robust and rugged as indicated by the %RSD values which are less than 2%. The results of Assay show that the amount of drug was in good agreement with the label claim of the formulation as indicated by % recovery (98.8% & 102.00% for zero order and 1st order Derivative respectively). Summary of validation parameters of proposed spectrophotometric method is shown in Table no.9. All the three methods which were developed were also evaluated.

Simultaneously this proved that all the three methods are equally good and capable of producing effective results. So for that any of the above three methods can be used for the determination of valacyclovir in pure and tablet formulation successfully.

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Design and Evaluation of Repaglinide Loaded Bio Lip Strips for Translabial Drug Delivery

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Abstract

Repaglinide is an oral blood glucose lowering drug which undergoes extensive first pass metabolism, extremely short half life of 1hr and low oral bioavailability(56%) making it a possible candidate for delivery through skin. The aim of this study was to explore the potentiality of lip skin as a novelistic platform due to its unique histology by formulating Repaglinide loaded lip strip using a novel bio material which was isolated from seeds of *Sesamum indicum* by simplified economical process. Repaglinide loaded bio lip strips were formulated by using *Sesamum indicum* biopolymer as a strip former and dextrose as a flexicizer. The formulated strip was subjected for various evaluation parameters like moisture content, folding endurance, swelling index, stability studies, *in-vitro* and *in-vivo* release. Our results revealed that the Repaglinide release was extended over a period of 24 hrs. This was confirmed by the *in-vitro* and *in-vivo* release data. The results are expressed as mean ± SEM values. Statistical significances were evaluated using t test. A value of $p<0.05$ was considered significant. The formulated strips are feasible for delivering Repaglinide through Translabial route.

Keywords: Translabial, Repaglinide, *Sesamum indicum*, strips.

Introduction

Lip skin is very unique. Lips are two fleshy folds surrounds the orifice of mouth consisting of three to five cellular layers of flat and scale like cells. Lip composed of skin and mucosa and devoid of hair follicles, sweat glands, sebaceous glands and melanin[1]. Unlike other skin the stratum corneum of lip skin is extremely thin or completely absent in most people. Translabial drug delivery can be used for both; local therapeutic effects on diseased lip skin as well as for systemic delivery of drugs. Translabial route avoids problems of gastric irritation, hepatic first pass metabolism, reduce the risk of systemic side effects and sustained the release of drug at the site of application[2-5]. The skin forms an excellent barrier against drug permeation, due to the rigid lamellar structure of the stratum corneum lipids. Our novel lip drug delivery sidesteps this barrier due to very less layers of stratum corneum. Repaglinide is a non-sulfonyl urea oral blood glucose lowering drug of the meglitinide class used in the management of Type II Diabetes mellitus[5-6]. Repaglinide is a BCS class II compound[7]. It lowers blood glucose by stimulating the release of insulin from the pancreas by closing ATP-dependent potassium channels in the membrane of the beta cells. This depolarizes the beta cells and opening the calcium channels and the resulting calcium influx induces insulin

secretion. Repaglinide has an extremely short half life of 1hr, low oral bioavailability (56%) due to extensive hepatic first pass effect[8]. Dosing frequency of Repaglinide is 0.5 to 4mg in 3 to 4 times a day. The bio strip of Repaglinide may be beneficial to the patients since it enhance the bioavailability due to avoidance of hepatic first pass metabolism, reduce dose frequency and adverse effects and maintaining un-fluctuating plasma concentration of Repaglinide. Sesamum indicum, belong to family Pedaliaceae. The seeds are exceptionally rich in iron, magnesium, manganese, copper, calcium and contain vitamin B1 (thiamine) and vitamin E (tocopherol). They contain lignans, including unique content of sesamin, which are phytoestrogens with antioxidant and anti-cancer properties. The aim of our research work was the formulation and evaluation of bio lip strip of Repaglinide using natural biomaterial (TB) for lip as a site for drug delivery.

Materials and methods

Repaglinide (assigned purity, 99.8%) was a gift sample from M/S Torrent Pharmaceuticals Ltd., Ahmedabad, India. Seeds of *Sesamum indicum* were purchased from market of Dehradun, Uttarakhand, India, Sodium carboxy methylcellulose (Na-CMC) and Hydroxy propyl methyl cellulose (HPMC) were purchased from Merck Specialties Private Limited, Mumbai, India. All other chemicals and solvents were of analytical grade.

Isolation of *Sesamum indicum* bio material:

Sesamum indicum seeds were procured from the local market. Novel biomaterial from *Sesamum indicum* was isolated by simplified economical process using acetone and purified by hot dialysis method using ORCHID scientific dialysis apparatus for complete removal of impurities like Chlorides and sulfates. The purified bio material was screened through 200# and stored for further research work.

Preparation of Bioadhesive Lipstrip:

Accurately 100mg of *Sesamum indicum* biopolymer(TB) was weighed and transformed into the mortar, to this 110mg of dextrose was added and triturated the mixture for a period of 5minutes after that 5mg of Repaglinide was incorporated in geometrical dilution pattern. Further 10ml of double distilled water was incorporated by adding drop by drop to the mixture with constant trituration. The mixture was subjected for magnetic stirring for a period of 10 minutes and sonicated at 400 Hz for 3 cycles of 60seconds each in order to form a colloidal mixture. The colloidal mixture was poured into Petridis having 6cm diameter and subjected for evaporation at room temperature for a period of 10hrs. Dried strips were carefully removed and it was cut into 2X2cm^2 and strips were placed over the adhesive backing membrane (Table 1). F7 and F8 are standard formulations.

Table 1: Composition of various batches of Repaglinide loaded bio-lip strips.

S.No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1	Repaglinide (mg)	5	5	5	5	5	5	5	5
2	*Sesamum indicum* biopolymer (mg)	100 (1%)	200 (2%)	300 (3%)	400 (4%)	500 (5%)	600 (6%)	--	--
3	Sodium carboxy methyl cellulose (mg)	--	--	--	--	--	--	400 (4%)	--
4	Sodium alginate(mg)	--	--	--	--	--	--	--	400 (4%)
5	Dextrose (mg)	110	110	110	110	110	110	110	110
6	Double distilled water(ml)	10	10	10	10	10	10	10	10

Drug- Excipient interaction study:

The pure drug along with other formulation excipients was subjected to interaction studies. Studies were carried out by dry as well as wet mixing of drug and excipients in the ratios 1:1, 1:3 and 3:1. Both types of mixtures were stored at room temperature and at 55°C in oven for three days. The appropriate dilutions were done with the help of methanol and phosphate buffer of pH 7.4 and samples were scanned for λmax using UV spectroscopy and result was reported.

The pure drug along with formulation excipients were subjected to interaction studies. The study was performed by using FT-IR spectroscopy. It was performed by mixing/grinding definite proportions of drug and excipients with a specially purified salt (potassium bromide) finely (to remove scattering effects from large crystals). The powder mixture was then pressed in a mechanical press to form a translucent pellet through which the beam of the spectrometer can pass. The FT-IR peaks were found and reported.

Characterization of bio-lip strips

Thickness:

The thickness of three randomly selected bio-lip strips was assessed at five (center and four corners) different places on a single patch of each formulation using a micrometer screw gauge and the mean value were calculated and reported[9].

Weight uniformity study:

Weight uniform study for all formulated bio-lip strips was performed by taken three randomly selected bio-lip strips from each formulation with surface area $1cm^2$ were used. Each strip was weighed individually on electronic balance. The study was performed thrice and average weights were calculated and registered[9-10].

Content uniformity:

All formulated bio-lip strips were evaluated for its drug content uniformity. From each

formulation the randomly selected strip (1cm^2) was transferred into a 100ml volumetric flask containing 7ml of phosphate buffer of pH7.4 and 1ml of methanol. The flask was stirred for 4 hrs on magnetic stirrer. A blank was prepared by using a drug free patch treated similarly. The solutions were filtered through a 0.45micro meter membrane. The drug content was then determined after proper dilutions by using an UV spectrophotometer (Shimadzu 1800)[9-10].

Folding endurance:

Folding endurance for all bio-lip strips containing Repaglinide was performed by using a strip of area 4cm^2 from each formulation. The selected bio-lip strip was subjected to folding endurance by repeatedly folding a strip at the same place until it broke. The number of folding required to break or crack a strip was taken as the folding endurance. This test was repeated thrice and overcomes was noted[11-12].

Swelling index:

Swelling study of all formulated bio lip strip was calculated by taken a bio strip from each formulation of size 1 cm^2 .the bio-lip strip was weighed on a pre weighed cover slip. It was kept in a Petri dish and 10 ml of phosphate buffer of pH 7.4 was transferred. After one hour, the cover slip was removed and weighed. The difference in the weights gives the weight increase due to absorption of water and swelling of bio-film. The change in weight was noted after 24 hrs. The procedure was repeated thrice and swelling index(S) was determined by using below formula.

Where, Xt - weight of the swollen bio strip after time t and Xo - original weight of bio strip[13].

$$\% S = (X_t - X_o / X_0)\ 100$$

Percentage moisture absorption (PMA):

Percent moisture absorption study for all formulated bio-lip strips was conducted by taking a 1cm^2 of Repaglinide loaded bio-lip strips. The bio-lip strips were transferred into a watch glass and it was placed in dessicator containing saturated solution of Aluminium chloride and kept a side for 72hrs. At the end the weight gained by the strip was determined. The study was repeated thrice and percentage moisture absorption calculated by using the below mentioned formula[14]

$$\text{Percentage moisture absorption} = [(\text{final weight} - \text{initial weight})/\text{initial weight}]\ X\ 100$$

.

Percentage moisture loss (PML):

Percentage moisture loss study for all formulated bio lip strip was performed by taking three 1cm^2 strips from each formulation. The strips were cut out and weighed accurately and kept in dessicator containing fused anhydrous calcium chloride for 72 hrs. At the end the weight loss by the strips were determined. The study was repeated thrice and percentage moisture loss calculated by using the below mentioned formula and reported[14].

$$\text{Percentage moisture loss} = [(\text{initial weight} - \text{final weight})/\text{initial weight}]\ X\ 100$$

Surface pH study:

The surface pH of the bio lip strips containing Repaglinide was determined by using a glass electrode. The bio lip strips was allowed to swell by keeping it in contact with 0.5 ml of distilled water for 1 hour at room temperature. The pH was measured by bringing the electrode in contact with the surface of the bio strip and allowing it to equilibrate for 1 minute. The experiments were performed in triplicate and average values were noted[15].

Water vapor transmission test (WVT):

WVT defined as quantity of moisture transmitted through unit area of strip in unit time. Glass-bottle (length= 5 cm, narrow mouth with internal diameter =0.8 cm) filled with 2 g anhydrous calcium chloride and an adhesive (Feviquick®) spread across its rim, was used in the study. The bio strip was fixed over the adhesive and the assembly was placed in dessicator in which 200 ml of saturated sodium bromide and saturated potassium chloride solution were placed. The desiccator was tightly closed. The weighed bottle was then placed in dessicator and procedure was repeated[16, 17].

$$WVT = W/ST$$

W is the increase in weight in 24 h; S is area of strip exposed (cm^2); T is exposure time.

Skin Irritancy:

Primary skin irritation studies were conducted with best two optimized patch in four rabbits. Rabbits were divided into two groups of two animals. Blank strip were applied on the lip of rabbits of group I which served as control and rabbits of group II received medicated strips on their lip. Strips were changed after 6hrs with fresh strips. The study was carried out for a period of 7 days and application sites were graded for redness, erythematic or irritation visually[18].

***In-vitro* diffusion study:**

The *IN-VITRO* drug diffusion was carried out in the M.S. diffusion apparatus. This was the static method and employed complete replacement of the sample. Dialysis membrane was tied to the terminal portion of the cylindrical donor compartment. A $1cm^2$ bio-lip strip was kept above the dialysis membrane in the donor compartment, and the receiver compartment was filled with 13 ml of diffusion medium. The complete sample was withdrawn at different time intervals and the receiver compartment was refilled with 13 ml of fresh medium. The amount of drug released was assessed by measuring the absorbance at 281nm using UV spectrophotometer (Shimadzu 1800).

***In-vivo* release study:**

The *in-vivo* release was performed in rabbits for the optimized formulation. The bio-lip strip was applied to the lip of rabbit and blood samples were taken from the ear vein at intervals of 2, 6,

10, 12 and 24hours to determine the concentration of drug in the blood plasma. Plasma was separated immediately by using centrifugation at 3000xg for 10min. The plasma was treated with 5ml methanol of HPLC grade, subjectected for sonication for 5 cycles and filtered through membrane filter. The drug content was estimated by injecting the filtrate into the HPLC column using methanol and phosphate buffer of pH 7.4 as mobile phase and at a rate of 1.2ml/min[19].

Stability studies:

Optimized bio lip strip was subjected to stability study. Bio strips were wrapped in Aluminum foil and packed them in glass vials. These strips were kept in an incubator (stability study chamber) maintained at 37±5°C and 75±5% R.H. for six months. The change in appearance, physical characteristics and release behavior of the stored strips were investigated after 1-6 months. The data presented were the mean of three determinants[20].

Results and discussion

Drug-Excipients Interaction study:

The drug interaction study revealed that there was no interaction between the drug and the excipients including the bio- material because there was no change in the λmax value which was observed to be 281 nm prior to the test and after the test, which confirmed that there was no interaction between the drug and excipients. All the FT-IR peaks of Repaglinide were present as such in the spectra of grinded drug and excipients mixture. No observable signs of drug interaction were seen. It was conclude that none of the excipients had a detrimental effect on the drug and could be safely used for the formulation of the bio-films.

Evaluation parameters of Repaglinide loaded bio-lip strips:

The formulated strips were smooth and translucent in appearance. The average thickness of all prepared bio-lip strips ranged from 0.43±0.03 to 0.83±0.02 mm. Thus the proportional gain in weight of strips was observed as the thickness of strips increased. The values were uniform for the strips within the respective group of formulation type. This depicts that the strips cast was uniform. Surface pH for all formulations was found to range from 6.32 ± 0.17 to 6.63 ± 0.15. Since range of the pH of strip is near to the skin pH. No skin irritation was expected. The folding endurance of strips was found in the range of 108 ± 5.8 to 155 ± 6.3. High folding endurance values for strips indicates high mechanical strength of strips. This is highly desirable because it would not allow easy dislocation of the strips from the site of application or breaking of strip during administration. No skin irritation, redness or erythema was observed during primary skin irritation studies with all formulations. Rest observations of evaluated parameters are shown in table 2.

Table 2: Evaluation of various batches of Repaglinide loaded bio-lip strips.

Formulation	Content uniformity	Moisture uptake	VTR	Weight uniformity	Moisture content	Swelling index
F1	93.48±0.32	2.72±0.23	7.63±0.35	24.38±0.36	0.36±0.078	112.58±0.41
F2	96.41±0.48	3.12±0.36	7.62±0.28	31.45±0.28	0.98±0.085	127.42±0.53
F3	96.69±0.38	3.78±0.32	6.54±0.54	37.72±0.34	0.98±0.31	138.54±0.63
F4	91.50±0.28	4.21±0.28	7.43±0.61	28.62±0.33	0.83±0.42	153.27±0.48
F5	90.98±0.32	4.18±0.41	7.07±0.63	26.78±0.27	0.82± 0.36	117.67±0.32
F6	95.45±0.33	4.36±0.46	6.81±0.66	32.83±0.24	0.81± 0.27	131.75±0.56
F7	91.36±0.50	4.42±0.46	3.36±0.69	26.66±0.20	1.36±0.17	151.42±0.29
F8	93.82±0.43	3.28±0.27	4.81±0.29	21.52±0.27	0.98±0.24	119.68±0.44

***In-vitro* release:**

In-vitro release of Repaglinide from different strips is shown in fig. no. 01. Formulations (F3, F7 and F8) released >80% of the drug before 10hrs. Formulation F6 showed the maximum release of 94.33% at the end of 24hrs. Formulation F5 showed slower drug release, and showed maximum drug release of 87.32% after 24hrs. We could not detect any relationship between the drug release profile and polymer composition may be due to release mechanism which governed by diffusion as well as erosion controlled, since our biomaterial is slightly soluble in water. The release data of the tested strips were analyzed on the basis of Krosmeyer-Peppas equation and Higuchi kinetics (by BIT-SOFT 1.12: drug release kinetics with model fitting). Coefficients of correlation (R^2) were used to evaluate the accuracy of fit. The R^2 value for Higuchi and Peppas kinetic models were calculated and compared. All the tested formulations gave good fit to the Krosmeyer-Peppas model. All formulations showed non-Fickian drug release ($0.5<n<1$). The in-vitro release obtained by Translabial strip were significantly ($p<0.05$) different from standard formulations. On the basis of above parameters and used concentration of biopolymer F2 was selected as the best formulation. The *in vitro* studies have shown that this is a potential drug delivery system for Repaglinide with considerable good stability and release profile.

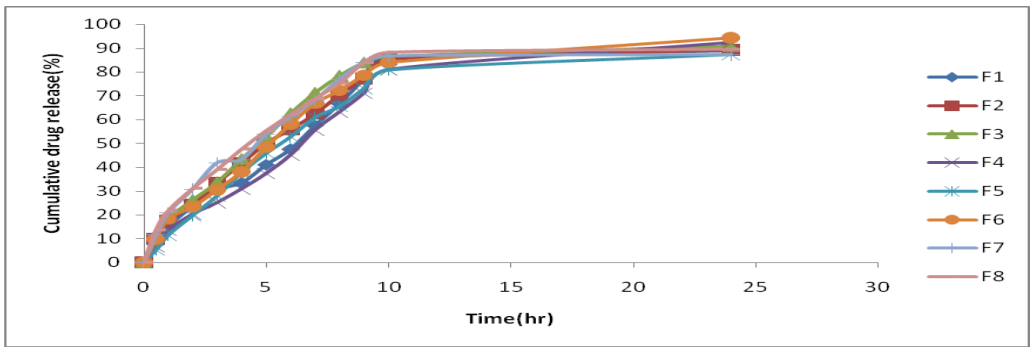

Figure 01: In-Vitro drug release profile for batch F1-F8

Stability study:

At the end of stability study, the tested strips showed similar drug content as observed at the beginning of the study. They also showed insignificant difference for in-vitro drug release. All optimized strips showed satisfactory flexibility and elastic properties during and at the end of the accelerated stability period. These all indicated that there were no influences on the chemical and physical stability of the formulation during the test period.

Conclusion

In the present study bioadhesive bio-lip strips based on *Sesamum indicum* biomaterial was developed, which released the drug over the required period of time (12 h) which would prevent first-pass metabolism. Thus, an attempt of formulating a stable bioadhesive bio-lip strip of Repaglinide for treatment of diabetes using novel biomaterial was made by optimization technique. Thus, this natural biomaterial could be a promising excipient for systemic delivery of drugs through labial route and other transdermal route.

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Formulation and Evaluation of Isoflavone Tablets using Natural Gums as Release Modifier

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Abstract

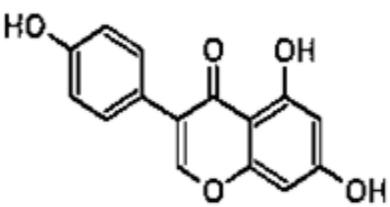
The objective of the present research work was to develop sustained release matrix tablets of Isoflavone using natural gums as xanthum gum and karaya gum. Varying ratios of drug and polymer like 1:1 and 1:2 were selected for the study. Nine batches were prepared by wet granulation method. After fixing the ratio of drug and polymer for control the release of drug up to desired time, the release rates were modulated by combination of two different rates controlling material. The granules were evaluated for angle of repose, bulk density, tapped density, bulkiness, compressibility index and Hausners ratio. The tablets were subjected to weight variation, hardness, friability and drug content test. Invitro release studies revealed that F9 formulation was able to sustain the drug release for 10 hours (84.1% ±1.85). Fitting the invitro drug release data to kinetic analysis, all the formulations followed the mechanism of both diffusion and erosion. The in vitro release of isoflavone from the developed formulation was compared with the marketed one using statistical analysis based on different evaluation parameters. The marketed product is available as tablet containing isoflavone 60mg. Stability studies (40±2ºC/75±5%RH) for 3 months indicated that isoflavone was stable in the matrix tablets. The FTIR study revealed that there was no chemical interaction between drug and excipients.

Keywords: Isoflavone, xanthan gum, karaya gum, 0.1N HCl

Introduction

Soy isoflavone is a type of flavonoids contained in soybeans and is particularly prevalent in soy germ. Soy products containing isoflavones are claimed to decrease cholesterol, prevent osteoporosis, ameliorate the effects of menopause, and lower the risk of certain cancers, including prostate, breast, and colon cancer. Some particular soy isoflavones, such as genistein and daidzein, have also been reported to inhibit the growth of different types of cancer cells in culture.

Isoflavones are among the most promising potential anticarcinogenic compounds in soybeans. Epidemiological studies indicate that consumption of soybean-containing diets is associated with a lower incidence of certain human cancers in Asian vs. Caucasian populations[1].



The chemical structure of isoflavones is very similar to that of estrogen. Because of this similarity in structure, they can interfere with the action of estrogen. Depending on the type of estrogen receptor on the cells, isoflavones may reduce or activate the

activity of estrogen. Isoflavones can compete with estrogen for the same receptor sites thereby decreasing the health risks of excess estrogen. They can also increase the estrogen activity. If during menopause the body's natural level of estrogen drops, isoflavones can compensate this by binding to the same receptor, thereby easing menopause symptoms[2]. Epidemiological studies indicate that dietary isoflavones provide health benefits for men and women.

The following potential health benefits are attributed to isoflavones:

- Ease menopause symptoms
- Reduce heart disease risk
- Protect against prostate problems
- Isoflavones improve bone health
- Reduce cancer risk

Chemically isoflavone is 7-O-(6″-O-malonyl-β-D-glucosides), it has usual dose of 40 mg isoflavones/day, oral bioavailabilty 45%. It is sparingly soluble in water. Isoflavones are transformed by bacteria in the intestinal flora during digestion. Lower absorption in the intestine has been observed following a lengthy intake of antibiotics or in the case of diarrhea. This can result in a reduction of the protective functions of these substances for the body[3]. In order to obtain a regular absorption of isoflavones, the intake isoflavones rich foods or isoflavones supplements must be spread during the day.

The objective of the present research work was to develop sustained release matrix tablets of Isoflavone using natural gums as xanthum gum and karaya gum. Varying ratios of drug and polymer like 1:1 and 1:2 were selected for the study. The *in vitro* release of isoflavone from the developed formulation was compared with the marketed one using statistical analysis based on different evaluation parameters. The marketed product is available as tablet containing isoflavone 60mg[4].

Materials and methods

Soyisoflavone was procured as gift sample from Yash pharmaceutical private Ltd. Roorkee Haridwar (Uttarakhand). Xanthan gum and Karaya gum were obtained from M/s H.B. Gum Industries Pvt. Ltd., Kalol, and all other solvents and reagents were of analytical grade.

Drug Excipients interaction study

The knowledge of drug excipients interaction is useful for the formulation to select appropriate excipients. The described Preformulation screening of drug Excipients interaction requires only 5mg of drug in a 50% mixture with the excipients to maximize the likelihood of obscuring an interaction. Drug Excipients interaction study was done using FT- IR. (Table 1&2, Figure 1& 2)

These all bonds and group are present in ISOFLAVONE. The major peaks of spectra show the compound identification. –C-H bound give maximum spectra peaks. Compound was found

ISOFLAVONE.

C-H, C-O, C=O and C-H stretch bounds are characteristics peaks of Isoflavone. No special identification peaks found in the mixture of Isoflavone, Xanthan gum and Karaya gum. This showed that there is no interaction found between these compound. All these peaks are due to presence of isoflavone.

Thin layer chromatography

Thin layer chromatography is an important analytical tool in the separation, identification and estimation of different drugs[5].

Application of the sample

The solution of Isoflavone (0.1%w/v) was made in ethanol. About 5µl sample was spotted by capillary tube on the pre coated silica gel G-TLC plates by keeping a distance of about 2 cm above the base of the plate. Allow it to dry in air.

Development of the chromatogram

The plate was then placed in TLC chamber previously saturated with appropriate solvent system of chloroform: methanol: water: acetic acid (60: 30: 10: 0.5, v/v/v/v) for the development of chromatogram, the plate was removed and the spot was observed under the UV chamber at the short wavelength 254nm, the principal spot in the chromatogram obtained. The Rf value was calculated and tabulated. The results of other preformulation studies are tabulated here (Table 3).

Drug identification test

Analytical method

Isoflavone can be estimated by UV spectrophotometrically in pharmaceutical formulation. A solution of Isoflavone in ethanol gives maximum absorbance at λ_{max} of 254 nm.

Evaluation of mixed blend of drug and excipient [6], [7]

All the ingredients were passed through mesh no 85. Granules were prepared by wet granulation method and was evaluated for flow properties as follows (Table 5)

Angle of Repose

Angle of repose was determined by using funnel method. The granules were poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of heap (r) was measured and angle of repose was calculated using the formula:

Angle of repose = tan Ø h/r

Bulk Density

Bulk density was determined by pouring a weighed quantity of granules into graduated cylinder and measuring the volume and weight. The bulk density was calculated using the formula.

BD = Weight of the powder / Initial Volume

Tapped Density

Weighed quantity of granules were taken in measuring cylinder and it was tapped untill the constant height obtained. The tapped density was calculated using the formula.

Tapped density = Mass of powder \ Volume of powder after tapping

Carr index: The Carr's index was calculated using the formula.

Carr index = (Tapped density – Bulk density) / Tapped density

Preparation of Tablets

Sustained release matrix tablet containing 60mg of soyisoflavone were prepared by wet granulation technique. All the ingredients was passes through sieve # 85, weighed accurately, mixed in mortar and pestle and granulated using PVP K-30 in isopropyl alcohol as granulating aid. The granules obtained were dried in oven at 50 ^{0}C for 2 hours. After drying, granules passed through sieve #25 to obtained uniform size granules. The dried granules were passed through sieve # 44 and lubricated with magnesium sterate by further blending for 3 min and finally talc was added to the blend. Compression was done after sufficient lubrication. Matrix tablets were prepared using single punch tablet machine using 8mm deep concave punch[8]. (Table 4)

Evaluation of prepared tablets[9-14]

Weight Variation

Twenty tablets were selected randomly from each formulation and weighed individually using a digital balance. The individual weights were compared with the average weight for the weight variation. (Table 6)

Thickness variation

Ten tablets from each formulation were taken randomly and their thickness was measured with a vernier caliper (25×1 mm, lest count= 0.01 mm).

Hardness

Hardness of the tablets was measured using the Monsanto Hardness Tester (Pharmalab, Ahmedabad, India).

Friability

The friability of a sample of twenty tablets was measured using a USP type Roche friabilator (Pharmalab, Ahmedabad, India). Pre-weighed tablets were placed in a plastic chambered friabilator attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were then dusted, reweighed and percentage weight loss (friability) was calculated using the formula.

% Friability = (Loss in weight / Initial weight) × 100

Drug Content

Three tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately average weighed amount of tablets triturate was taken for

analysis. Samples were transferred to different volumetric flasks and were diluted up to the mark using 0.1 N HCl. The content was shaken well and kept for 30 minutes for dissolving the drug completely. The mixtures were filtered and appropriate dilutions were made. The drug content in each tablet was estimated at lamda max 254 nm against blank as reference.

Swelling behavior of matrix tablets

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of formulation F-2, F-5 and F-7 was studied. One tablet from each formulation was kept in a Petridish containing pH 6.8 phosphate buffer. At the end of 1 hour, the tablet was withdrawn, soaked with tissue paper, and weighed. Then for every 2 hours, weights of the tablet were noted, and the process was continued till the end of 8 hours. % weight gain by the tablet was calculated by formula;

$$S.I = \frac{Mt - Mo}{Mo} \times 100$$

where,

S.I = swelling index; Mt = weight of tablet at time't' and Mo = weight of tablet at time t = 0

In vitro drug release study

In vitro drug release study of the samples was carried out using USP – type II dissolution apparatus (Basket type).In the dissolution flask to maintain the temperature of 37 + 0.5 ^{0}C and rpm of 50. One tablet was placed in each basket of the dissolution apparatus. The apparatus was allowed to run for 10 hours.

Samples measuring 5 ml were withdrawn after every hours using 10 ml pipette. First 2 hrs in 0.1 N HCl and then in Phosphate buffer 7.4.The fresh dissolution medium (37 ^{0}C) was replaced every time with the same quantity of the sample. Collected samples were analyzed at 254 nm using 0.1 N HCl and 7.4 Phosphate buffer as blank. The cumulative percentage drug release was calculated.(Figure 3)

Statistical Analysis

Each tablet formulations were prepared in duplicate and each analysis was duplicated. In vitro release profile of prepared formulation was compared with marketed isoflavone tablet and tested for significance by using independent t-test with the aid of SPSS-12.0. Difference was considered significant when $p<0.05$.

Stability Studies

The stability of selected formulations was tested according to International Conference on Harmonization guidelines for zones III and IV. The formulations were stored at accelerated (40$\pm$ 2^0/75$\pm$5% RH) and long term (30$\pm$ 2^0/65$\pm$5% RH) test conditions in stability chambers (Thermotech TH-7007, India) for three months following open dish method. Stability studies indicate that there is

no major difference in hardness, friability and swelling time after storing formulations for six months. The dissolution profile (Fig.4) of fresh and aged Isoflavone matrix tablet showed no significant effect on drug release ($p > 0.05$). Stability studies show that the physical and chemical properties of the tested tablets were not altered significantly ($p>0.05$) and all the test formulations were found to be stable. [15]

Results and discussion

In the present study isoflavone tablets were prepared by wet granulation technique and were studied for their hardness, friability, drug content,swelling index and in vitro release profile. Xanthan gum and karaya gum was selected as a natural polymer for the preparation of sustained release tablet due to its low biological half life and poor water solubility properties. The effect of formulation variables such as different natural polymers and different percentage concentration and there combining swelling property was studied.

Precompressional studies

Precompressional parameters of granules like angle of repose in range (25.98 to 29.84), % compressibility in between (16.87 to 22.26) and Hausner's ratio was calculated which is in the range of (1.18 to 1.28) the result indicates good flow property and compressibility.

The prepared tablets were found white colored, circular biconvex. Tablets were free from cracks, depression, pinholes, etc. Whole surfaces were smooth and elegant in appearance. Size of isoflavone tablet was studied with the help of vernier calipers. For all batches tested tablets were found to be uniform in weight.

The thickness of the tablets was ranged from 5.12 mm to 5.75 mm.The hardness and percentage friability of the tablets of all formulation remained in range of 4.12 to 4.75 and 0.59 to 0.76 % respectively which was in the range of official standard.

For all the batches tested the percent of Isoflavone in the compressed tablets was within 70.25 -99.67 % of the theoretical label claim (350 mg / tablet).Swelling index of all the formulation were found in range of 37.5 to 72.85. Maximum swelling index 72.85 was found in formulation F-9, which contain equal amount of xanthan gum and karaya gum. Karaya gum was used as a release retarding polymer due to its more swelling behavior.

In vitro drug release study of all the formulation was carried out using 0.1N HCL for initial 2 hrs and in pH 7.4 phosphate buffer for next 8 hrs in which drug release was completed in that time. The mixture of xanthan gum and karaya gum extend the release of drug more than individual use of natural gum.

F-7, F-8 and F-9 have the combination of xanthan gum and karaya gum in the 15%, 20% and 25% respectively. F-7 gives 76.3% drug release, F-8 gives 71.4% drug release and F-9 gives 70.4% drug release in 8hrs. It means that as the concentration of combined gum increase the time of drug release becomes delay.

F-9 formulation release 70% drug in 8hrs, in which 27% drug release in 0.1 N HCL in 2 hrs. But other formulation releases the drug more than 70% in 8hrs and more than 27% drug release in 0.1 N HCL in 2hrs and that is why F-9 formulation extend the maximum time release for the sustained formulation because the blend of karaya and xanthan gum showed more swelling behavior due to high viscosity of karaya gum. (Figure 5 & 6)

The above plot showed that drug release was faster initially and it becomes extended as time passed. Blend formulation containing preparations are much better than the karaya gum and xanthan gum for the sustained release formulations.

The *in vitro* release of isoflavone from the developed formulation was compared with the marketed one using statistical analysis.The test result showed that there is no significant difference in the in vitro release profile between prepared tablet batches and marketed one. ($p>0.05$)

Kinetic Analysis

The release rate kinetic data for all the formulations were shown in Table 8. When the data were plotted according to zero order, the formulations showed a high linearity, with regression coefficient values (R2) between 0.9873-0.9945. Diffusion is related to transport of drug from the dosage matrix into the *invitro* study fluid depending on the concentration. From the release exponent in the Korsmeyer-Peppas model (n = 0.7168) it could be suggested that the mechanism that led to the release of soyisoflavone was an anomalous transport.(Table 7 & Figure 7)

Table 1: The FT-IR spectra peaks found in Isoflavone

Functional group & bound	Nature	Range (cm^{-1})
C-H Rocking	W	600-900
C-O Stretch	M	900-1300
-C-H Bonding plane	Ms	1300-1500
C=O Stretch	S	1600-1900
-C-H Stretch	S	2700-3300

Table 2: The IR spectra peaks found in Isoflavone, Xanthum Gum, Karaya Gum

Functional group & bound	Nature	Range (cm^{-1})
C-H Rocking	W	600-900
C-O Stretch	M	900-1300
-C-H Bonding plane	Ms	1300-1500
C=O Stretch	S	1600-1900
-C-H Stretch	S	2700-3300

Table 3: Results of Other Preformulation Studies

TLC (Rf Value)	0.76
Loss on Drying	0.67%
Log P	0.85

Table 4: Compositions of 350 mg Isoflavone Matrix Tablet. (Weight in mg).

Formulation Code	Drug	Xanthan Gum	Karaya Gum	MCC	PVP K30 3%	Mag. sterate 1%	Talc 2%	Total
F1	60	52.5	-------	216.5	10.5	3.5	7.0	350
F2	60	70.0	-------	199.0	10.5	3.5	7.0	350
F3	60	87.5	-------	181.0	10.5	3.5	7.0	350
F4	60	-------	52.5	216.5	10.5	3.5	7.0	350
F5	60	-------	70.0	199.0	10.5	3.5	7.0	350
F6	60	-------	87.5	181.0	10.5	3.5	7.0	350
F7	60	26.5	26.5	216.5	10.5	3.5	7.0	350
F8	60	35.0	35.0	199.0	10.5	3.5	7.0	350
F9	60	43.75	43.75	181.0	10.5	3.5	7.0	350

Table 5: Evaluation of Isoflavone Granules

Batch no	Bulk Density (g/cm^3)	Tap Density (g/cm^3)	Angle of Repose (^{0})	Carr's index (%)	Hausner's ratio
F1	2.01	2.53	26.36	20.56	1.26
F2	1.99	2.56	28.48	22.26	1.28
F3	1.97	2.37	28.39	16.87	1.20
F4	2.02	2.46	25.98	17.88	1.22
F5	1.92	2.47	27.47	22.26	1.28
F6	1.96	2.38	28.48	17.64	1.21
F7	1.99	2.41	29.84	17.43	1.21
F8	1.94	2.43	28.75	20.16	1.25
F9	2.05	2.42	29.75	15.28	1.18

Table 6: Post Compressional Parameters of Isoflavone Tablet

Formulation code	Hardness (Kg/cm^2),	Friability (%), n=10	Wt Variation (%), n=10	Thickness (mm),n=5	Drug content (%),n=3	Swelling Index
F1	4.75± 0.22	0.75±0.08	1.94± 0.1	5.23± 0.2	99.78± 0.08	37.5±0.21
F2	4.45± 0.25	0.69±0.02	2.23± 0.20	5.12± 0.2	94.89± 0.06	43.05±0.20
F3	4.12± 0.32	0.68±0.04	2.92± 0.13	5.25± 0.2	93.42± 0.06	66.94±0.24
F4	4.25± 0.10	0.63±0.08	2.79± 0.12	5.37± 0.2	90.48± 0.11	39.8± 0.21
F5	4.58± 0.18	0.64±0.06	3.01± 0.12	5.75± 0.2	85.59± 0.12	47.38±0.48

F6	4.45± 0.22	0.59±0.04	3.26± 0.02	5.38± 0.2	83.64± 0.14	69.93±0.21
F7	4.34± 0.20	0.72±0.03	2.87± 0.12	5.27± 0.2	76.30± 0.02	40.37±0.20
F8	4.57± 0.12	0.76±0.08	1.98± 0.02	5.29± 0.2	71.41± 0.08	46.83±0.08
F9	4.70± 0.24	0.68±0.07	3.45± 0.02	5.35± 0.2	70.43± 0.22	72.87±0.08

***(N=3)**

Table 7: Kinetics of drug release of F7/F8/F9 formulation

kinetic parameter	F7		F8		F9	
Zero order	R	K	R	K	R	K
	0.9039	6.15121	0.9874	8.3157	0.9817	7.9165
First order	0.8500	-0.1071	0.9755	-0.1673	0.9462	-0.1579

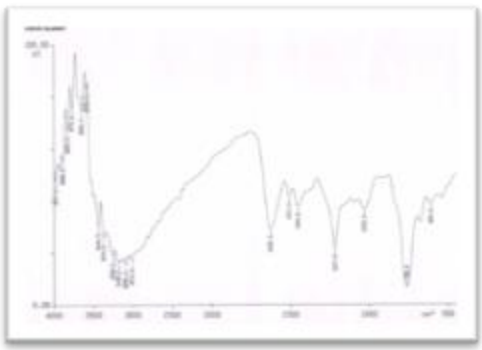


Figure 1: FT-IR spectra of Isoflavone drug.

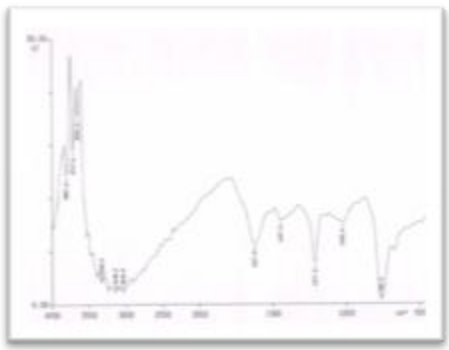


Figure 2; FT-IR spectra of Isoflavone, Xanthan Gum and Karaya Gum

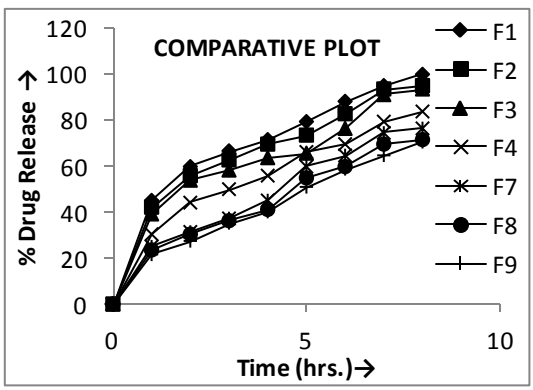


Figure 3: in vitro Release profile of Matrix tablets of Isoflavone.

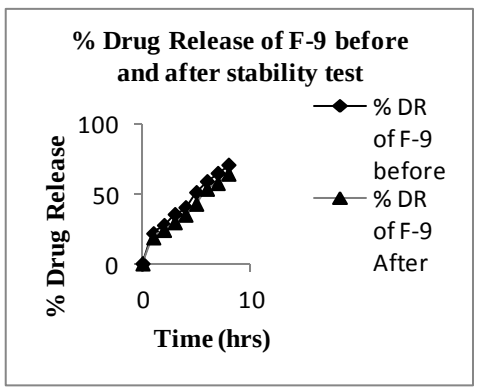


Figure 4: in vitro release profile of Isoflavone Matrix Tablet (Fresh & aged)

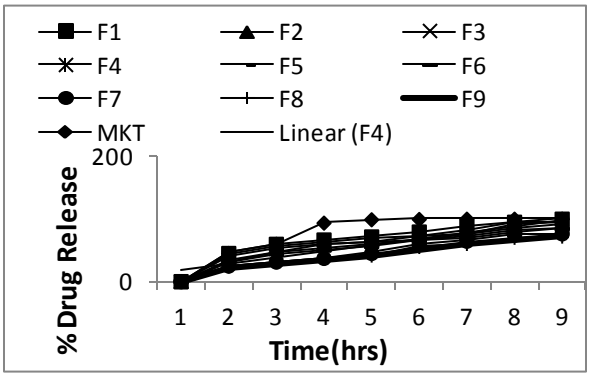


Figure 5: Comparison of In vitro release profile of prepared Isoflavone Matrix Tablet with marketed Tablet

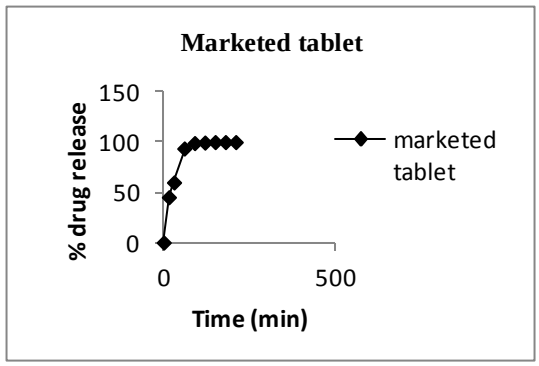


Figure 6: Percentage drug release of marketed tablet of isoflavone

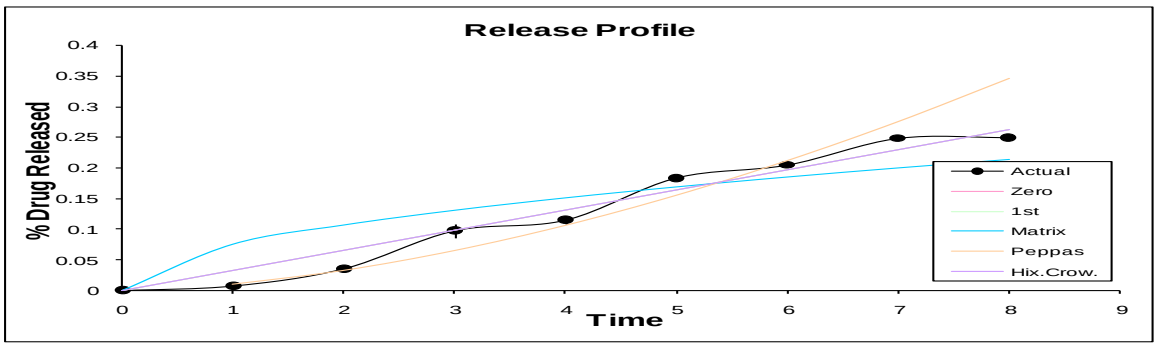


Figure 7: Drug release through the different kinetic model

Conclusion

The results of experimental studies of isoflavone matrix tablets proved that the granules showed good flow properties, tablet evaluation tests are within the acceptable limits, IR spectral analysis proved that there was no drug- polymer interaction, the kinetic studies revealed that all the formulations followed zero order drug release and stability studies revealed that all the formulations were found to be stable.

Acknowledgement

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Jackfruit Jam: Preparation Nutritive Values and Storage Stability

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Abstract

Jackfruit extract has good gelling capacity, but its potential has not been exploited. The present study aimed to evaluate the physicochemical characteristics of jackfruit and to study their suitability for jam processing. The jam prepared from extracted pulp was packed into glass jars and stored under three temperatures (room temperature (25±5ºC), incubator (37ºC) and at cold temperature (7ºC) to examine any possible deterioration in physicochemical properties of the Jam. Chemical and organoleptic tests as well as changes in sensory qualities during storage period were carried out. In addition, the microbial load of the stored prepared jams was determined by the enumeration of total viable count, yeast and mold concentrations. The sensory evaluation results indicated that jam was very stable in colour, taste and overall acceptability if stored under cold temperature (7ºC) for 12 months as it was found to be free from microorganisms. The jams were found free from microorganisms in the other two storage temperatures i.e. room temperature and incubator temperature too up to 8 months, clearly demonstrated its potential for commercialization.

Keywords: Jackfruit, Jam**,** Total soluble solids**,** Nutritive value, Storage stability

Introduction

Jackfruit (*Artocarpus heterophyllus*) is a horticultural crop and grown in almost all parts of the India. It is widely used for culinary purposes and preparation of pickles when the fruit is in tender (unripe) stage. The increase in jackfruit production and rapid loss of the product due to their short shelf life and underutilization due to insufficient processing facilities, have stimulated search for the suitable maturity stage of fruit at which it can be harvested for the development of food products. Determination of the fruit maturity and harvesting time may accelerate the process and product development from this fruits and thus, prevent the loss of fruits.

The fruit color changes from green to yellowish green during the ripening process due to the conversion of fruit pigments like chlorophylls, anthocyanins and carotenoids[1]. Finally the colour of outer skin of the ripe fruit turned to yellow. The ripe Jackfruit consists of yellow flesh, pith and large numbers of bulbs inside the fruit that has carbohydrates, proteins and minerals in sufficient quantity. The ripe fruit also contains macronutrients like calcium, magnesium and micronutrients such as vitamins, minerals and organic acids.

Jam made from different types of fruits is a popular food items among the local population. It is usually prepared from cooked fruit or vegetable, sugars, citric acid and pectin[2]. Quality of jam

prepared depends on physicochemical characteristics as well as the acceptance of fruit or vegetable. The processing of jackfruit into jam is therefore, highly appreciable in order to channelize the underutilized jackfruit. Kansci et al studied the ripening effect of different varieties of mango (Abusamaka, Galb Altour and Magloba) on the composition and the suitability for jam processing, and reported that due to the their higher starch contents, all jams prepared with pre-ripe mangoes were more viscous than ripe mango jam processing[3].

Commercial production of fruit jams is subject to standard formulations of fruit type, sugar content, adjusted acidity and pectin content. Jam is a semisolid food made from not less than 45 % (by weight) fruit and 55% (by weight) sugar having 65% or above total soluble solids (TSS)[4]. Additional amount of pectin, acid, flavoring and coloring agents may be added to improve the setting and taste of jam if any deficiencies exist in the fruits. Optimum pH conditions are found near 3.2 for gel formation. High sugar content of jam suggests that these products should resist spoilage by microorganisms. Potassium metabisulphite (KMS) or sodium benzoate was usually used as a preservative (class II preservatives) to prevent the microbial spoilage of jam. However, standard formulations were developed according to their end use, consumer preferences, market demand, food laws, buyer's specifications and economic utilization of inputs required.

Materials and Methods

Collection of Jackfruits and extraction of pulp

Freshly harvested, plant ripened and sound fruits were selected. These fruits were cleaned and kept in cool temperature prior to further treatment and analysis. Different edible parts of fruits like bulbs, seed, and pith (core) were segregated. The bulbs were subjected to colloidal mill to extract the pulp.

Estimation of TSS, pectin and acidity

TSS of pulp was measured with hand refractometer (BM, India) with measurement range of 0 to 50°Brix. The juice of jackfruit pulp was obtained by homogenizing and filtration or directly pressing the pulp using cotton pad. The 2 drops of juice of jackfruit pulp was poured on the lower part of the prism fitted on bottom side of the refractometer and closed properly with upper part of prism. A separation line appeared in the middle of dark and bright area. This line corresponds to the scale of reading in ^{0}Brix. The zero reading (reference) is set with water[5].

Presence of pectin in the given pulp is essential to know whether the pulp alone can form the gel during Jam production or additional pectin has to be used for jam setting. Therefore, to evaluate the pectin content in the pulp, about 10 g of pulp was taken into a glass tumbler and 30 ml methyl alcohol (95% pure) was added gently along the sides of the tumbler and mixed it by rotating the tumbler carefully. The mixture was then allowed to stand for 2 minutes. The mixture turned to a

single clot in middle layer if rich in pectin, fragmented clot if pectin present in moderate and only small dispersed granules in case of poor or negligible pectin. Addition of sugar in the Jam preparation was linked with pectin content in the pulp. 1-1.25 kg of sugar per 1.0 kg of pulp if the pulp rich in pectin, 0.5 kg or less of sugar per 1.0 kg of pulp if moderate quantity of pectin may be required to form good quality of jam. If the pulp has very poor pectin, required amount of pectin should be added from out side[6].

Acidity was estimated by the method described by Tiwari and Vidyarthi[7]. In this method 10 g of pulp/jam were suspended in distilled water to make 100 ml sample solution. Solution was filtered through Whatman filter paper to remove any suspended matter. A 10 ml aliquot was taken in 100 ml conical flask and titrated against N/10 NaOH using few drops of 1% phenolphthalein solution as indicator. The total acidity (as citric acid) was calculated by following equation:

$$\%\text{Titrable acidity} = \frac{\text{Titre x Normality of alkali x Volume made up} \times \text{Eqvt. Wt. of acid} \times 100}{\text{Volume of sample taken For estimation x Weight or volume of sample} \times 1000}$$

To estimate Ascorbic acid in sample, 10 g sample (pulp/jam of jackfruit) was taken in 100 ml volumetric flask and volume was made up with 3% HPO_3 solution followed by filtration through filter paper. A 2 ml of filtered sample taken in a 100 ml conical flask was titrated with dye solution (50 mg of sodium salt of 2, 6-dichlorophenol indophenol in 150 ml hot distilled water with 42 mg of sodium bicarbonate). Titration was completed when end point (pink colour persist for at least 15 second) appeared as method described by Nielsen[8]. The amount of ascorbic acid present in the sample was calculated as per following formula:

$$\text{Ascorbic acid (mg/100g)} = \frac{\text{Titre x Dye factor x Volume made up}}{\text{Volume of filtrate taken x Weight or volume of sample}} \times 100$$

Preparation of Jam

Sugars and citric acid in adequate quantity were added during cooking of extracted pulp in stainless steel pan. Pectin (0.6–1.0%) blended with a little amount of warm pulp was added to the mixture and cooked further till mixture reached 68% TSS (°Brix). KMS was added just before end of cooking[2]. Various Jam samples were prepared by varying composition of pulp, sugar and citric acids with or without additional quantity of pectin (Table 1). The physicochemical characteristics of these jam preparations were also studied.

Table1: Jams recipe adopted

S.No.	Pulp (kg)	Sugar (kg)	Citric acid (g)	KMS (mg)	Water (l)	Pectin (Added) %
Group A						
1.	1.0	0.50	6.0	30	1.0	Nil
2.	1.0	0.75	9.0	45	1.0	Nil
3.	1.0	1.0	12.0	60.0	1.0	Nil
Group B						
4.	1.0	0.50	6.0	30	1.0	0.75
5.	1.0	0.75	9.0	45	1.0	0.75
6.	1.0	1.0	12.0	60.0	1.0	0.75

Storage stability studies on Jam

The prepared jams were packed into glass/pet jars and stored under three temperatures (Room temperature (25±5ºC), incubator (37ºC) and at cold temperature (7ºC). For jackfruits, the pulp extraction percentage, total soluble solids, acidity, Vitamin C content, were estimated.

The pectin content of jackfruit was also determined according to Hez et al[9]. For the prepared jams, colour, acidity and total soluble solids were determined using the methods described by various researchers. The prepared jams were coded and stored for the evaluation of microbial growth and changes in sensory qualities during storage period evaluated sensory and organolypicaly for colour, flavour, taste, consistency and overall acceptability, by a panel of 9 trained judges according to the method of Thekoronye and Nagoddy[10].

Estimation of microbial load in Jam

Fruit jam was analyzed for microbial load by the plate count method described by Diliello[11]. Dilution tubes containing 9 ml distilled water were autoclaved at 15 psi for 15 min. 1.88 g High plant count agar was dissolved in 100 ml of distilled water and heated to boil. The agar medium was autoclaved at 15 psi for 15 min. One g of jam sample was taken in one dilution tube containing 9 ml of pre-autoclaved distilled water and mix properly with vortexing. Subsequent serial dilutions of the sample were made upto 5^{th} dilution. One ml each of diluted sample was poured on the petriplates containing 20 ml pre-autoclaved agar medium at about 55^0C (before solidification of agar) and mixed properly. These petriplate(s) were incubated at 37^0C for 24 h for developing the colony forming unit (CFU) on the medium surface. The microbial load (CFU/g) in the jam samples was calculated by number of colonies developed multiplied by dilution factor.

Results

Preparation of Jam from ripened Jackfruit

Jam shall contain minimum soluble solids not less than 68.5% (w/w) that may be achieved by fruit pulp and additional sugar. About 0.6 to 1.0% pectin is also required for gel formation and satisfactory structure[12]. Therefore, it is prudent to evaluate the TSS and pectin content in the fruit pulp in order to assure good quality of jam preparation. The fruit consist of 35.5 % pulp, 13.75% seed, 46% peel and rind and remaining as unusable fruit parts. The pulp in ripened fruit contains TSS about 29^0 Brix, valuable amount of vitamin C and other nutritive ingredients. Pleasant and acceptable color and flavor were noticed and found suitable for preparation of jam like products. An economical formulation can be developed by using minimum necessary sugar to pulp ratio and adjusted solids between 60% and 65% (w/w). The Jam was prepared from the fruit pulp by two methods (Table 1). In one method three sets of sugar, citric acid concentrations were taken along with 1 kg pulp and 1 kg water without adding additional pectin (Experiment 1 to 3) and in the second method 0.75% pectin of the pulp were added additionally to form rigid gel structure (Experiment 4 to 6). Even without additional pectin, the gel with good setting was observed in experiment 1 due to the fact the pectin present in the pulp was sufficient to carry the sugar added. In other two experiments either gel was not formed or gel formed without setting may be due to less pectin in comparison to the sugar added. In all experiments conducted by method 2 in which additional pectin was added, the good quality of gel was formed with good setting. Surprising in experiment 4 the rubber like gel (too hard) was formed due to less sugar in comparison to total pectin present. Finally the experiment 6 was carried forward for subsequent studies due to its quality in terms of gel formation and its setting. The total soluble solids, total acidity and vitamin C (mg/100g) were 68^0 B, 1.0% and 15.2(mg/100g) respectively in the final jam.

Stability of physicochemical properties of jams during storage at different temperatures:

Effect of storage temperature on stability of jam and its physicochemical properties has been studied at three temperatures (cold temperature 7 ^{0}C, room temperature and incubator temperature 37 ^{0}C). There was no change in TSS observed for the three different storage temperatures, upto 8 months of storage, and a very slight decrease in TSS (8 °Brix**)** was noticed after 16 month (Fig 1a). Similarly the vitamin C content in the jam was also intact upto 8 months of storage in all the three temperatures and decreased subsequently (Fig 1b). However, an insignificant increase in acidity was observed in 8^{th} month (1.2%) of jam stored at room temperature and in 12^{th} month (1.41%) at room temperature (Fig 1c). The significant decrease in TSS and vitamin content as well as increase in acidity in case of jam stored at incubated temperature for 16 months may be due to microbial activity in the jam (Table 2).

Stability of color, flavor and taste of jam during storage at different temperatures

In order to assess the quality of jam on storage the jam samples were stored at three temperatures

as mentioned earlier and the change in color, flavor and taste was recorded on an interval of 4 months. The results are shown in Table 3-5. There was no change in color of jam in 12 month storage at cold temperature, 8 months in other two temperatures. However, the color changes to slight brownish yellow to blackish after 16 months of storage (Table 3). Similarly there was no off flavor was noticed during eight months of storage at the three temperatures. A slight alcoholic flavor was observed in 12 months of storage at room temperature and also at incubator temperature. Significant off flavor was observed after 16 months of storage in the two samples (Table 3). The taste of these jams was also intact up to 8 months of storage at all three temperatures; however slight sour taste was developed in 16 months of storage (Table 5). The commercial samples of other fruit jam, available in the market, are mostly stable for 6 to 12 months only. Therefore, the jam prepared by present method has the potential for its commercialization.

Table 2: Chemical changes during storage

Duration of study	Total Acidity (mg/100g)			Vitamin C (mg/100g)			T.S.S °Brix		
	CT	RT	IT	CT	RT	IT	CT	RT	IT
Nov.2010	1.0	1.0	1.0	15.2	15.2	15.2	68	68	68
Feb.2011	1.0	1.0	1.0	15.2	15.0	15.0	68	68	68
June.2011	1.0	1.2	1.0	15.1	14.07	14.51	68	67	68
Oct.2011	1.0	1.32	1.41	14.8	13.2	13.03	68	65	63
Feb.2012	1.32	1.43	1.50	12.3	11.35	10.51	63	62	60

Table 3:

Duration of study	Change in color			Change in flavor		
	Cold temp. (7°C)	Room temp. (25±5°C)	Incubator temp(37°C)	Cold temp. (7°C)	Room temp. (25±5°C)	Incubator temp. (37°C)
Nov.2010 (0 Month)	No Changes	No Changes	No Changes	No Changes	No Changes	No Changes
Feb.2011 (4 Month)	No Changes	No Changes	No Changes	No Changes	No Changes	No Changes
June.2011 (8 Month)	No Changes	No Changes	No Changes	No Changes	No Changes	No Changes
Oct.2011 (12 Month)	No Changes	Brownish yellow	Blackish on Top	No Changes	Slightly Alcoholic	Alcoholic
Feb.2012 (16 Month)	Brownish yellow	Blackish on Top	Black	Alcoholic	Off flavour	Off flavour

Table 5:- Change in tastes

Duration of study	Cold temp (7°C)	Room temp (25±5°C)	Incubator temp (37°C)
Nov. 2010 (0 Month)	No Changes	No Changes	No Changes
Feb. 2011 (4 Month)	No Changes	No Changes	No Changes
June. 2011 (8 Month)	No Changes	No Changes	No Changes
Oct. 2011 (12 Month)	No Changes	Slightly acidic	Sour
Feb. 2012 (16 Month)	Sour, pungent & rancid	Sour	Sour and pungent

Table 6:- Microbial load in CFU/g of jam by direct plate count (x 10^5)

Duration of study	Cold temp (7°C)	Room temp (25±5°C)	Incubator temp. (37°C)
Nov. 2010 (0 Month)	0	0	0
Feb. 2011 (4 Month)	0	0	0
June. 2011 (8 Month)	0	1	0
Oct. 2011 (12 Month)	0	4	7

Microbial stability of jam during storage at different temperatures

No detectable yeast and mold was observed during the 12 months of storage of jam at cold temperature. However, only few colony forming units (CFU) has been observed in prolong storage at room temperature and incubator temperature due to insufficient amount of preservative (KMS) and stabilizer (Table 6).

Discussion

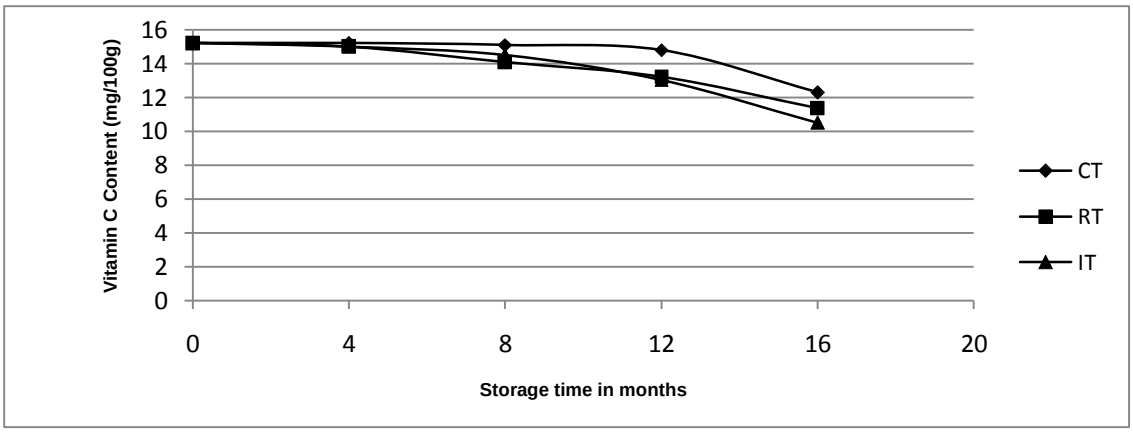
In order to know jelling properties of Jackfruit a pre-screening process was carried out with and without pectin. Jam samples prepared with and without pectin gave better gel (result not shown) and final sample was selected for further analysis. The jelling property of Jackfruit as anticipated is due to presence pectin and solid matter in the rind and middle lamella of the fruit. Varied composition of pulp, sugar and fixed quantity of pectin was used to prepare different jam samples (Table 1) and physicochemical characteristics of these formulations were studied. Total acidity, vitamin C and total soluble solid contents of the jam samples were determined at 4 months interval for a period of 16 months in order to assess the possible deterioration of these quality parameters during storage. The soluble solids did not significantly change during storage or among storage temperatures. These results are in agreement with Ndabikunze et al., who reported no significant changes in the soluble solids in all fruit jams formulations during his study on the production of jam from indigenous fruits using baobab[13].

A gradual decrease in ascorbic acid concentration in samples stored at room temperature

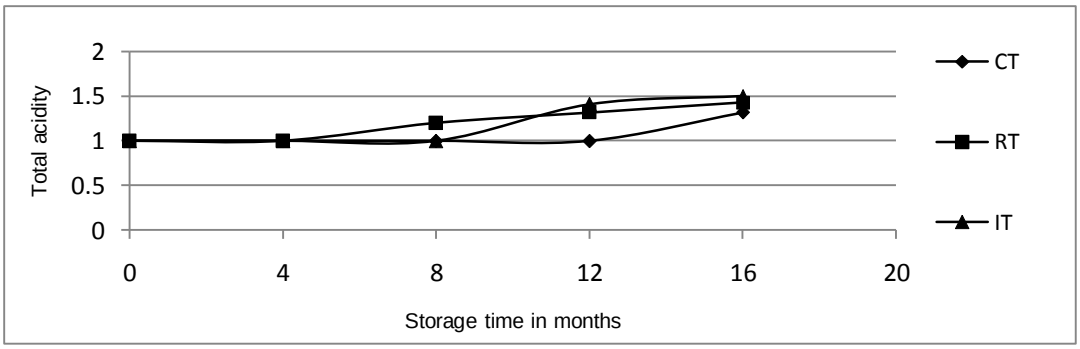
and in incubated temperature was observed (Table 2). This decrease might due to oxidation taking place within the sample as well as enzymatic catalytic reaction taking place within the jam mass during storage, Jawaheer et al., observed similar effects between jam made from guava fruits[14]. Another principal cause of ascorbic acid decrease might be residual oxygen present within the container head space (assuming glass ware was impervious to oxygen) assisted by degrading activities of light. In this study, gradual increase in total acidity was noticed from 8 months in the formulated jam stored at different temperature except jam stored at cold temperature (7ºC). In a study conducted by Khan et al., it was revealed that the acidity increased during storage of strawberry jam[15]. Sogi and Singh reported that this increase in acidity might be due to ascorbic acid degradation and hydrolysis of pectin[16].

The rate of color loss was slower in samples stored at cold temperature (7ºC) than the samples stored at comparatively higher temperature. It was noticed that the no significant change even after12 months of storage at cold temperature (7ºC) but after 8 Months of storage a brownish yellow and blackish colour on the top of the jar was found in jam samples stored at room temperature and incubated temperature respectively. Sensory evaluation of jam revealed higher deterioration in colour, appearance and flavour on 12 and 16th month of storage at higher temperature (25±5ºC and 37ºC) compared to jam stored at 7ºC, the same types of findings reported by Vidhya and Narain in their study on development of preserved products (jam and fruit bar) from under-exploited wood apple[17].

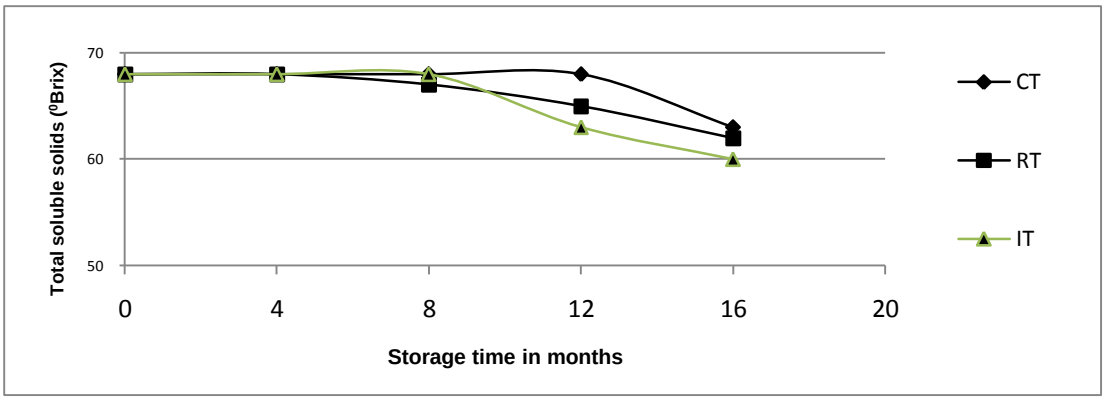
The microbial growth at various time intervals and the increase in CFU/g of the jam samples in prolong storage indicated that the sugar and SO_2 content added in jams was not sufficient to prevent microbial spoilage during storage. The growth was found to be highest at the 8 months of the storage period in the sample stored at 25±5ºC and 37ºC, which may be attributed to the variability in the temperature and the chemical changes, specifically change in total soluble solids and concentration of SO_2 of the samples. Chacko et al, reported almost similar type of results in their study on effect of storage conditions on the microbial quality of fermented foods[18]. High sugar content of jam suggests that these products should resist spoilage by microorganisms. However, even 68% sugar solids is not a guarantee against the growth of certain molds and yeasts, particularly molds. Potassium meta-bisulphite (SO_2) or Sodium Benzoate (Benzoic acid) may be used as a preservative (class II preservatives). Benzoic acid and SO_2 are generally regarded as safe up to a maximum permitted level of 40 ppm and 200 ppm respectively in India[19]. There is no preservative that is completely effective against all microorganisms present in a given foodstuff. In theory, one should be able to combine various preservatives to achieve a broader spectrum and increased antimicrobial action[20].



(a) Total soluble solids



(b) Vitamin C content



(c) Total acidity

Figure 1: Effect of storage temperature on product stability

CT-Cold Temperature 7ºC RT- Room Temperature 25±5ºC; and IT- Incubator Temperature 37ºC

Conclusion

The present study aimed to develop a process for preparation of fruit jam from under-utilized jackfruit that cultivated in almost all part of India. The Jam prepared has significant nutritive values required for growth of human being. The quality of jam in terms of total soluble solids, ascorbic acids has been investigated intermittently during its storage at three temperatures. The results of this study clearly demonstrated the use of jackfruit for jam preparation and its potential for commercialization. The jam preparation from ripen jackfruit will not only provide the new products to the consumer but also help the farmers to earn the money which may otherwise waste due to perishable nature of fruit.

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Dispensing the Prescription

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Preamble

A **prescription** (℞) is a health-care programme that governs the plan of care for an individual patient and is implemented by a qualified practitioner. As medications have increasingly become pre-packaged manufactured products, the term "prescription" now usually refers to an order that a pharmacist dispenses and that a patient takes certain medications. Prescriptions have legal implications; it implies that the prescriber takes responsibility for the clinical care of the patient and in particular for monitoring efficacy and safety. As medical practice has become increasingly complex, the scope and meaning of the term "prescription" has broadened to also include clinical assessments, laboratory tests, and imaging studies relevant to optimizing the safety or efficacy of medical treatment.

Significance

The process of dispensing a prescription is a highly responsible job where extreme care is required to ensure safety in dispensing. An effective system of safe dispensing with checking and re-checking of prescription before dispensing medicines is not only very important but also inevitably necessary in the interest of health and happiness of the patient. It is pharmacist's professional responsibility to ensure that prescriptions are properly dispensed and any potential medication error is completely avoided. As human error can not be eliminated completely it is essential that all prescriptions written by the doctor are scientifically and technically checked by the pharmacist in each and every respect before it is dispensed. The element of re-checking by the pharmacist reduces prescription errors to a great extent and prevents mishaps or medication errors. There are seven rights which need to be practiced by the Pharmacist i.e. right choice of drug, right dose, right dosage form, right route of administration, right frequency of administration, to right patient, at right time. These are the basic requirements of clinical pharmacokinetics to provide safe and effective medication and eliminate medication related complications.

Background

A sizeable proportion of untoward effects of medicines are due to irrational use or human error and are therefore preventable as emphasized above. The main ones are:

- Wrong diagnosis of the patient's condition
- Prescription of the wrong drug or wrong dosage of the right drug

- Undetected medical, genetic or allergic condition in the patient which might cause a bad reaction to the drug
- Self-medication
- Lack of adherence to the prescribed course of the drug
- A large number of different drugs being taken by the patient (polypharmacy), which may interact

Introduction

Medical errors, defined as a preventable adverse event or effect of care, are a leading cause of death in the United States—exceeding deaths attributable to motor vehicle accidents,[1] breast cancer,[2] and heart failure.[3] They include inaccurate or incomplete diagnosis or treatment, as well as when an appropriate method of care is executed incorrectly.[4] Human error has been implicated in nearly 80 percent of adverse events that occur in complex healthcare systems. The vast majority of medical errors result from faulty systems and poorly designed processes versus poor practices or incompetent practitioners.[5]

First credited with initiating an industry-wide call to improve patient safety, a 2000 Institute of Medicine (IOM) report, "To Err is Human: Building a Safer Health System," estimated that medical errors result in between 44,000 and 98,000 preventable deaths and 1,000,000 excess injuries each year in U.S. hospitals.[6] Most of the errors cited in the IOM report were due to problems in the health care system rather than individual failures.

A 2006 follow-up to the IOM study found that medication errors are among the most common medical mistakes, harming at least 1.5 million people every year. In 2000 alone, the extra medical costs incurred by preventable drug related injuries approximated $887 million—and the study looked only at injuries sustained by Medicare recipients, a subset of clinic visitors.[7]

In the United States, reporting medical errors in hospitals is a condition of payment by Medicare. However, an investigation by the Office of Inspector General, Department of Health and Human Services released January 6, 2012, found that most errors are not reported and even in the case of errors that are reported and investigated changes are seldom made which would prevent them in the future.[8]

Statistics

The statistics relating to medication and health care industry errors in USA are as under:

- Medication errors occur in about 1 of 5 doses in hospitals.
- Medication errors cause at least one death every day. (FDA)
- 1.3 million People sustain injury from medication errors every year. (FDA)
- It is estimated that 7,000 people die each year from medication errors.
- More people die a year from *medical* errors than from motor vehicle accidents.

- Adverse drug events cause more than 770,000 injuries and deaths every year. This costs up to $5.6 million per hospital.
- Patients who suffered adverse drug effects remained in the hospital an average of 8-12 days longer than those who did not. These extra days added $16,000 - $24,000 more to the patients hospital bill.
- A recent study was conducted at two prestigious teaching hospitals, which showed that two out of every 100 admissions experienced preventable adverse drug reactions. This cost the hospital $4,700 per admission.
- Preventable adverse drug reactions cost the healthcare industry $2 billion annually.
- Infusion devices account for up to 35% of all medication errors that result in significant injuries. The most common errors (in order) are manually programming incorrect infusion parameters, failure to ensure the right patient receives the right medication, and tampering of infusion parameters by unauthorized users.

Common causes

- Incorrect diagnosis
- Prescribing the wrong medication
- Drug interactions and reactions
- Dose miscalculations
- Incorrect drug administration
- Lack of patient education
- Job related stress
- Improper training or education
- Sound-alike or look-alike drug packaging

Conclusion

In view of the prevailing conditions and dangers posed by modern medicines, if not used judiciously and accurately, the role of pharmacist has become significantly important. He has to dispense the prescription applying perfect knowledge, expertise and skill with adequate communication ability to facilitate rational and proper use of prescribed medicines.

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Family Planning Scenario in Bihar – A Journey Ahead

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Abstract

The current challenges to health are many but family planning is one issue which is touching more lives than any other health issues. And this is one area which has not only implications on health scenario of any country but has larger effect on Country's economy and social growth. Every aspects of growth can be directly or indirectly correlated to increasing population which is a true and hard fact. In-spite of greater effort made by country like India, the Population Stabilization is far away to reach. Family Planning statistics are different in various state of the country among which state like Bihar are populous and alarming. The growth indicators are poor and unmet need of family planning, basket of choices limited choice of method, unaddressed family planning needs and queries, lesser involvement of male, reach to the rural masses especially in hard to reach areas, accessibility and availability of methods less updated knowledge among service providers and lack of counseling skills, less awareness among society are various unlimited reasons which needs serious attention by the policy makers. There is need to revive the existing policy and need to reintegrate the program in a newer framework which has more decentralized and community approach through this paper authors has reviewed the family planning statistics of Bihar in comparison to national standards, area which need attention and various recommendation and suggestion like Contraceptive Technology Update (CTU) Training of cadre of service Providers, method specific counseling, follow up including management of side effects, strengthening Village Based Institutions, promotion of Social Marketing to increase accessibility and availability of Family Planning Methods, to increase community based provisioning of Family Planning services including counseling through ASHA and AWWs, involving groups at community level for strengthening Family Planning services, utilizing the Village Health & Nutrition Day (VHND), ensuring Contraceptives Supplies, RCH (Reproductive Child Health) Camps, equipping sub-center, PHCs (Primary Health Centre's, CHCs (Community Health Centers) & FRUs (First Referral Unit) with basic minimum facilities to provide Family Planning services, ensuring quality of care in Family Planning Service, monitoring and data collection, building partnerships, collaboration with media, convergence with other department, community mobilization-strengthening of ASHA (Accredited Social Health Activist) , IEC (Information, Education and Communication) and BCC (Behavior Change Communication) and ensuring post abortion Family planning counseling.

Keywords: Unmet need of family planning, limited choice, Population Stabilization, basket of choices, decentralized approach, CTU Training, VHND, ASHA, IEC and BCC

Introduction

India was the first country in the world to formulate Family Planning Program in 1952 but this program has got the most set back in India as we are still struggling with problems related to increased population every year. Since 1950's the family planning program in India has undergone variety of forms. The passive, clinic-based approach of the 1950s, gave way to a more proactive, extension approach in the early 1960s. The late 1960s saw the emergence of a "time-bound", "target-oriented" approach with a massive effort to promote the use of IUDs and condoms. This was followed by even more forceful "camp approach" to promote male sterilization in the 1970s. The excesses of these campaigns lead to a severe backlash from which it took years for the program to recover. After re-christened as Family Welfare Program in 1978, maternal and child health services began to receive greater attention under the program's plan of action. The centrally funded program has been providing the states additional infrastructure, manpower and consumables needed for the delivery of services.

In the 1990s, Government of India began to reorient the program in the light of recommendations made by a subcommittee of the National Development Council, an expert group headed by Dr. M. S. Swaminathan, and more specifically to address the concerns expressed at the International Conference on Population and Development held at Cairo in 1994. Following a major review undertaken with the support of the World Bank and other agencies in 1994-95, method-specific Contraceptives targets were abolished and the emphasis shifted to decentralized Planning at district level based on community needs assessment, and implementation of programs aimed at fulfilling unmet needs. The first phase of the Reproductive and Child Health Program was launched in 1997 as a flagship program that covered the entire gamut of safe motherhood, child health and RTI/STI diagnosis and care. The National Population Policy (NPP) articulated the new broad-based approach towards population stabilization, and set long-term policy goals. A National Population Commission was also set up under the chairmanship of the Prime Minster of India to review, monitor and give directions for the implementation of the NPP, and to promote inter-sectoral coordination (Government of India Planning Commission, 2007)

Family planning- situation analysis of bihar

Bihar's Population as per the 2001 census is 82.9 million and during the 1991 census it was 21.8 million – an addition of 5.1 million in a decade. It is the third most populous state in India. The Population density in the State is 880 persons per sq. km., which is more than double the national average of 324 persons per sq. km. The State has recorded the highest decadal growth during the nineties. While all-India decadal growth rate of population was 21.34%, the population of Bihar rose by 28.45% between 1991 and 2001. (Government of India Planning Commission, 2007)

Table 1: Health Indicators of Bihar

Important health indicators	**Unit**	**Bihar**	**India**
Population (2001)	Million	82.88	1027.02
Decadal Growth (1991-01)	Percentage	28.43	21.34
Population Density (2001)	Per Square Kilometer	880	324
Maternal Mortality Ratio (MMR) (2005-06)	Per Lakh Live Births	371	301
Infant Mortality Rate (IMR) (2005)	Per Thousand Live Births	61	58
Total Fertility Rate (2005-06)	Per Thousand	4.2	3
Life Expectancy at Birth (1991-03)	**Year**	**Bihar**	**India**
Birth rate (2005)	Per Thousand	30.4	23.8
Death Rate (2005)	Per Thousand	8.1	7.6
Child Sex Ration (0-6 years) (2005-06)	Per Thousand	942	927
Important health indicators	**Unit**	**Bihar**	**India**
Male		61.6	61.8
Female		59.7	63.8
Full Immunization(2005-06)	Percent	33	44
Human Development Index (2001)	Index	0.367	0.472

Source: A report of the special task force on Bihar, 2007

Aim of the study

The aim of the study is to explore the Family Planning Scenario of Bihar, review the statistics and bottlenecks and suggest a future roadmap to improve the current scenario.

Rationale of the study

Around 40% of the population in Bihar is below poverty line. The major health and demographic indicators of the State like infant mortality rate (IMR), maternal mortality ratio (MMR), total fertility rate (TFR), etc. are much higher than the all-India level and reflect a poor health status of the State. The Human Development Index (HDI), a composite of literacy, life expectancy and per capita income, has increased for Bihar like the rest of India. But the State still lags at 0.367 compared to the Indian average of 0.472.Based on the indicators primarily related to primary health care infrastructure and reproductive and child health care, the State ranks 35th in the country (DLHS 2002-04).

The decadal Population Growth Rate during 1991-2001 was higher in Bihar (28.43%) compared with the national average (21.34%). The Total Fertility Rate is 4 (NFHS -3) as against 3.7 (NFHS- 2) which is much higher than the national average 2.6. The performance level of different districts show variations ranging from high levels to low levels of achievement. The current use of contraception has shown a gradual increase from 23.5% (NFHS-2) to 34.1% (NFHS-3). This is

however much lower than the national average of 56%, with birth spacing use dismally low at 8%. The unmet need for spacing is 23.1%, which is much higher than the national average of 6.35. Family planning is an essential component of primary health care and reproductive health and plays a major role in reducing maternal and newborn morbidity and mortality. This study has been done to see all the aspects of family planning Situation of Bihar and analyze the bottlenecks in the program and suggest the journey ahead for a more prosperous Bihar.

Materials and methods

Various national and international articles and papers has been reviewed to analyze the family planning scenario of Bihar. The literature reviewed is presented here:

The principal national goal in India since independence has been to improve the quality of life for its people. The most pressing problem presently faced by the nation, however, is its high rate of population growth. Despite intensive efforts on the part of the government to check this growth, levels of acceptance of family planning and health and MCH services use remain low. **(Population Council 1993)**

As per **IIPS and ORC Macro 2000** and **NFHS 2** study report nationally, nearly one half of currently married women (48%) were using some method of contraception in 1998-1999. Contraceptive prevalence varied widely among states, from less than 30% in Bihar, Meghalaya and Uttar Pradesh to more than 60% in Delhi, Haryana, Himachal Pradesh, Kerala, Punjab, Maharashtra and West Bengal.

As per **Ms Sandhya study in Year 2004**, she recommended that an expanded reproductive health program must address men both in terms of their own health needs and in terms of their shared responsibility as partners, husbands and fathers and should not be limited to promoting the use of male contraceptive methods. The role of male health workers who could play an active role in promoting male involvement also needs to be clearly defined (Sandhya, 2004).

As per the study of **Hassan & Nisar, 2012** reveals that the extent of knowledge of contraceptive methods has been highest in the religion of Buddhism and Jainism, while, the Christians witnessed the lowest knowledge of contraceptive methods among all the major religious communities. Moreover, there were significant differentials in the adoption of sterilization between each of the religious groups, highlighting the lowest use of sterilization by Muslim women and highest by Buddhist women.

Martorell R et al (2012) Maternal underweight and anemia are highly prevalent in Bihar, especially among adolescent girls aged 15 to 19 years. Although numerous programs and platforms exist for delivering efficacious interventions for improving maternal nutrition, the coverage and quality of these interventions are low.

Results

Despite great progress over the last several decades in Bihar the current trend in family planning shows low level of acceptance of Family Planning Methods, especially spacing methods. The current unmet need for family planning (NFHS 3) in Bihar is about 23.1 % of which need for spacing is about 10.7% and need for limiting is 12.4% which needs to be met through programmatic interventions.

The major issues affecting the implementation of the Family Planning program are as follows.

- Lack of integration of the Family Planning programs with other RCH components, resulting in dilution of roles, responsibilities and accountability of program managers both at state and district levels.
- Failure of the program to effectively undertake measures to increase median age at marriage and first childbirth.
- Inability of the program to alter fertility preferences of eligible couples through effective behavior change communication (BCC).
- Over emphasis on permanent family planning methods such as, sterilization ignoring other reversible birth spacing methods that may be more acceptable to certain communities and age groups.
- Due to high prevalence of RTI/STD, IUDs are not being used by majority of women.
- Continued use of mass media to promote family planning practices despite evidently low exposure to mass media in Bihar, leading to lower exposure of family planning messages in the community, particularly among rural and socio-economically disadvantaged groups.
- Weak public-private partnerships, social marketing to promote and deliver family planning services.(Public Private Partnership is improved since 2008-09. 102 Nursing homes in 20 districts are accredited to conduct Family planning operations . In 2008-09 accredited private Nursing homes are expected to conduct more than 50-60 thousand family planning operations in the state. From April, 2008, 223000 sterilization conducted till Jan, 2009 of which 40,000 are conducted by the accredited private Nursing Homes.

Discussion

With the above reflection on Family planning scenario in Bihar it is quite evident that there are barriers in accessing Family Planning Services and major ones are:

1. **Poor access to family planning methods and poor quality of Family Planning Services:** Therefore there is a need to provide skilled based training to the Service Providers and also to provide them an up to date with recent developments in the contraceptive technology, so that they can provide good quality Family planning Services

2. **Limited Knowledge of Family Planning methods especially Spacing methods**: Female sterilization is the most widely known method of contraception followed by male sterilization. The awareness for spacing methods is relatively limited among both women and men.

3. **Gender Inequalities : Opposition from Husband:** There have been some efforts to promote the use of male methods such as vasectomy and condoms still nationally less than one in five currently married women reported discussing family planning with their husbands (IIPS and ORC Macro 2000). Hence there is need to focus on involvement of male in family planning.

4. **Limited access to and availability of service:** A recent survey of health facilities across the country reports that most primary health center were not adequately staffed and only 16 percent of PHC had physicians trained in conducting sterilization and only two third had at least one paramedical staff trained in IUD insertion (IIPS, 2001).

Recommendation and suggestions

1. **Contraceptive Technology Update Training of cadre of service Providers:** The barriers in meeting contraceptive needs emphasize the need to conduct on regular basis the Contraceptive Technology Update Training of all cadres of Service Providers.
2. **Method specific counseling:** Counseling is the key elements of all the trainings and is also a key element of quality family planning services which allows the client to exercise informed choice, getting appropriate information about the correct and consistent use and successful continuation of the chosen contraceptives.
3. **Follow up including management of side effects**: For ensuring correct and consistent use of the chosen contraceptives, the clients should be given appropriate and adequate information about the follow up schedules and management of side effects.
4. **Strengthening Village Based Institutions:** It is important to strengthen Village based committees, Mahila Mandal and SHGs for increasing demand of Family Planning services from Government Health Delivery system especially health facilities at community level like PHC (Primary Health Centers), HSC (Health Sub Centers)
5. **Promotion of Social Marketing to increase accessibility and availability of Family Planning Methods.**

6. **To increase community based provisioning of Family Planning services including counseling through ASHA and AWWs**- Self Help groups, Mahila Mandals, Youth groups, peer group etc. will be strengthened to create awareness among community for Family Planning services in Government Service Delivery Points.
7. **Utilizing the Village Health & Nutrition Day (VHND)** as a platform to strengthen counseling, services and follow up of Family Planning users.
8. **Ensuring Contraceptives Supplies –** Non-availability/ stock outs of spacing methods such as pills and condoms leads to discontinued use of spacing methods, while ECPs have still not reached many facilities leading to unintended and unwanted pregnancies.
9. **RCH Camps-** The routine RCH camps if organized in collaboration with Government Department to offer comprehensive Family Planning services at district and block level which will include offering birth spacing as a focused intervention.
10. **Equipping sub-center, PHCs, CHCs & FRUs with basic minimum facilities to provide Family Planning services.** Health sub- centers should equipped with all logistical support of furniture's like examination table chair, table, almirah and equipments like IUD insertion Kits and other family planning products, registers and reporting formats etc. The sub-centers should have the necessary facilities to ensure privacy and confidentiality to the clients.
11. Operationalizing the **Quality Assurance Cell** at the State level, District level and facility level for better monitoring and supportive supervision.
12. **Monitoring and Data collection** Routine monitoring and quality of data collection needs to be strengthened. Supervision tools need to be put in place and supervisory cadres (LHVs, MOs and NGO workers involved in the supervision and monitoring tasks) need to trained on using the tools and providing timely feedback.
13. **Building partnership:** To strengthen family planning services by generating demand in communities through effective partnerships between Government departments (inter sectoral) and other private partners, including NGOs, corporate sector and private practitioners.
14. **Collaboration with Media-** Use of print and visual media to disseminate information on advantages of family planning, including birth spacing and small family size should be emphasized.
15. **Community Mobilization- Strengthening ASHAs** who is a community health volunteer and interface of the community and a link between the community and the health delivery

system her responsibilities will include counseling eligible couples for the acceptance of spacing and terminal methods, as well as offering services and products for spacing and referring for limiting methods.

16. **Strengthening Village Health Committee and involvement of Gram Goshti (village meeting)-**Coordination between AWWs (Anganwadi Worker), ASHA, SHGs (Self Help Group) will be critical and will be undertaken by the VHC. This will enable complementing the services provided by each one of them for the healthy outcomes of the community. ***Gram Goshti*** (meeting of opinion leaders at village level on development issues) will be organized and such forums will be used to discuss and encourage small families, spaced pregnancies and health and social outcomes of Family Planning use.
17. **Participatory Monitoring & Evaluation** ; This will be the integral component in entire phase of the program and target group will be involved form beginning to the end to themselves evaluate the proposed study and its significance in improving their quality life.
18. **IEC and BCC activities-** IEC/ BCC activities will be strengthened through focusing on knowledge gaps, misinformation in community, concerns regarding family planning, at the same time emphasizing on the benefits of family planning, such as, health outcomes for mother and children amongst other advantages.
19. **Post Abortion FP counseling and services-** A very critical aspect to post abortion care is to counsel the women and her family on adopting a FP method to prevent any further unplanned and unwanted pregnancy, or case of repeated abortions.

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With the grace of almighty and support from family members this study has been conducted. Our special thanks to the office colleague for their bright ideas and inspiration to look into the insight of the proposed study. Thanks to the team at Ranchi University for their throughout encouragement and support .

Last but not the least the library at XISS and Ranchi University has been great help to access the materials and journals which was very enlightening and helped to shape the study in the desired form. Thanks again to our family members who has been a source of motivation for us.

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What is that Prevents Us from Being Healthy??

Dr. Suresh R. Saravdekar
Advisor, Government of Maharashtra

During last decade, Vibrant economic climate has propelled India from low income economies to the ranks of middle-income countries, Life expectancy of Indian people has increased from 50 to 60/ 80 years. And India is currently having Highest Younger Population.

"Ironically, even after 60 years of independence and positive economic trajectory, " The Indian Dream of Health is Wealth & National Health is National Wealth" is not only still in dismal state but Indian population today is living in a state of Paradox". Let us examine the following four situations that presently we observe in India.

The present health condition of Indian people can be summed up in following four situations.

Situation 1	Situation 2
A group of people facing lack of provision of basic requirements to keep healthy i.e. there is no provision of clean water, food, air, environment & sanitation	A group of people facing lack of provision of basic requirements to keep healthy i.e. there is no provision of clean water, food, air, environment & sanitation
Situation 3	**Situation 4**
A group of people for whom all basic resources are available but there is over utilization/ consumption of resources e.g. Over consumption of food causing obesity & obesity disorders like diabetes, arthritis, hypertension etc.	This is typical of India, where women willfully, adapt to male dominated values This is seen as on one end as half-starved Poor women and self starved Zero- sized skinny Rich women on the other end.

The overall health condition of Indian Healthcare is thus – On one side scarcity of income leading to ill health – on the other side abundance is also resulting to ill health. Thirdly, a situation seen very typically in poor countries - where the adaptation to wrong social values also leading to ill health of particular class of a society. Fourthly, most people want more income to be healthy and strive for it. Yet as Western Societies have got richer, their people have become ***no healthier.***

So, having known that more & more spending on medicalcare is not going to improve the health of the people (Though it is definitely going to be a profitable dealing!!!) , We need to look at this problem differently. We need to ask different questions to get a correct answer to this burning health problem faced by our country.

Which pays much bigger Dividends?

- -treating Malaria/Dengue or killing mosquitoes
- -treating TB/Swine flu or using mask/not spitting in public places
- -treating Polio/ diphtheria / whooping cough or vaccination
- -treating rabies or vaccinating dogs
- -treating Malaria/Dengue or killing mosquitoes

To come out of this fix, we need to consider a "Totally new approach" which is advocated by Nobel laureate Amartya Sen . What does it says?? There are basically two types of handicap which prevent people from converting their resources into desired positive outcomes.

- 1. Economic Handicap
- 2. Conversion Handicap

Now, let us look at the above mentioned "Four Indian Situations", in this context,

Situation 1-

People lack "Earning Capability" and therefore fail to even fulfill minimum needs of their life like food and good shelter to live in. This is "Economic handicap". What are the overall Effects of Economic Handicap on Health in India?

In India, there is more than 25% population living below poverty line , (77 % of which live on less than Rs. 20 a day) without sufficient food supply resulting in 70% children anemic & 56.2 % women having lower body mass index.

Lack of Health-Education- resulting in high infant & maternal mortality rates, Poor living conditions with lack of safe water, sanitation & personal hygiene resulting in 7,80,000 deaths /year

Who is responsible for this?

- State has to provide all basic necessary resources so as to come out of "Economic Handicap"
- State has to provide the skills & opportunities for earning
- State also has to provide clean water, food, air & environment to live in

Situation 2 and 3-

Having provided with basic needs still people lack the capability to covert the primary resources into positive health. This is **Conversion handicap**, because of which – People lack the capacity

1. to get *proper information* on different options

2. having proper information & known options , they lack the *capacity to attach correct value* to each option and

3. also lack *capacity of proper reasoning* before **choosing** a particular option.

What are the effects of "Conversion Handicap"?.

People choose Mobile/TV over building a toilet, Junk food over balanced diet, Physical appearance / external looks over right exercise (as a result we now see mushrooming of cosmetic surgery centers, beauty spas and massage centers all over the country)

Situation 4-

The hopelessly deprived people lack the courage to desire any radical change and typically tend to adjust their desires and expectations to what little they see as feasible. They train themselves to take pleasure in small mercies and adapt to wrong social values- e.g. Subdued housewives in deeply sexist cultures, Workers in exploitative industries and Oppressed minorities. This is **"Social Adaptation Handicap"**. What are the effects of this handicap in India?

- Skewed sex ratio of 914: 1000
- 56 % children still not fully immunized
- High Maternal Mortality Rate &
- High Infant (girl) Mortality Rate

Conclusions –

Rich people are not necessarily healthy because they lack the capacity to convert the available resources into healthy life. They are conversion handicapped. Poor people are not healthy because they lack the capacity to earn sufficient income (Economic handicapped) to be healthy and also lack capacity to convert that income into healthy life because of conversion handicap & some by additional social handicap.

A recent review of world health situation is published in the Lacent ,(a well acclaimed medical journal). The findings of the expert committee reported under this review article are not only shocking but unacceptable.

"Globally, all over the world, life expectancy has increased, but at the same time, the number of healthy years lost to disability has also increased in most countries, That is to say," "Life expectancy has increased but, Healthy Life Expectancy" (HALE) has decreased. Fewer people are dying but more live with **disability.** Essentially, what ails you isn't necessarily what kills you. "***We are finding that very few people are walking around with perfect health and that, as people age, they accumulate unhealthy conditions***,"

Having known all these startling facts, and concepts, now, we need to ask ourselves totally different, basic and fundamental questions about our health.

What is today's "Concept of Health"?

Today's definition of health is "Absence of Diseases or disorder is health". But most of the time, the diseases or disorder is an "End Point" or an "outcome" of long time neglected health.
e.g. Anemia is outcome of long standing Malnutrition or Obesity is outcome of long standing overeating . As against this there is another concept of health.

That is called as- **"Life-Course Theory of Health**". ***It says that events that happen earlier in life, whether they are stress or chronic disease, impact the course of an outcome.***

For example, only prenatal care doesn't necessarily improve birth outcomes. By the time a woman is pregnant, issues such as malnutrition and obesity leading to anaemia and chronic diseases respectively, impact the physical health of both mother and baby. Therefore, thinking about being healthy prior to pregnancy pays much bigger dividends than treating acute conditions once they occur. "The choices women make about their health -- whether about diet, exercise or even whether to breastfeed -- have profound impacts later on, not one but on **TWO LIVES**,"

Similarly, only spending on highly technological interventions like heart stents, valves, implants is not going to improve quality of health.

Thus spending time and money on Preventive Healthcare pays bigger dividends than spending on Medicalcare.

Present is an information era. People are well aware of the health hazards like stress, irregular eating habits, irregular routines, and exposure to pollution, chemicals, however, they are not aware of "How to get rid of it & have good healthy life". So the end result is that - they are taking Health by Default.

They have sufficient "Primary Resources" like money, time, health information, different options of making oneself happy, many friends, relations but don't know how to convert all these resources in to healthy, happy and peaceful life. So what is that prevents us from being Healthy?? And who is going to help us to come out of this handicap? None other than ourselves

We have to take the rein of our health in our own hands.

(In this context there is a programme available, called "Health Designing", which aimed at empowering the participants, to learn, access, anticipate and capture the unhealthy events in advance and make them capable to arrest , correct and control the by Quality Healthy Living outcome . Those who are interested may contact Dr. Mansi Kirpekar on mobile no. 09833032373)

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Manuscripts will be subjected to peer review process to determine their suitability for publication provided they fulfill the requirements of the journal. After reviewer's comments the revised manuscript should be submitted by e-mail or in CD prepared in MS Word.

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Manuscripts should be concisely written and conform to the following general requirements: Manuscripts should be typewritten in 1.5 space in A4 sized sheets, only on one side, with a 1.0 inch margin on both sides. Research Papers, should not exceed 8-10 pages, Review Articles, 12-15 pages and Short Communications, 4-5 pages. Pages should be numbered consecutively, starting with the title page and the matter arranged in the following order: Title, Name and Address, Abstract, Keywords, Introduction, Materials and Methods, Results, Discussion or Results and Discussion, Acknowledgements and References. All other section titles should be in capital letters while subtitles in each section shall be in bold face lower case.

TITLE PAGE - Title page should contain title of the paper in bold face, title case (font size 14), names of the authors in normal face, upper case (font size 12) followed by the address(es) in normal face lower case. The author to whom all correspondence be addressed should be denoted by an asterisk mark.

ABSTRACT - Start on a new page after the title page and should be typed in single-space to distinguish it from the Introduction. Abstracts should briefly reflect all aspects of the study, as most databases list mainly abstracts. Short Communications as well as Review Articles should have an Abstract.

KEYWORDS – 4 to 5 Keywords related to topic

INTRODUCTION - Start immediately after the Abstract, as the next paragraph, but should be typed in double-space. The Introduction should lead the reader to the importance of the study; tie-up published literature with the aims of the study and clearly states the rationale behind the investigation.

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If should be about 15 pages long, contain up-to-date information, comprehensively cover relevant literature and preferably be written by scientists who have in-depth knowledge on the topic. All format requirements are same as those applicable to full papers. Review articles need not be divided into sections such as materials and Methods and results and Discussion, but should definitely have an abstract and introduction, if necessary.

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The journal publishes exciting findings, preliminary data or studies that did not yield enough information to make a full paper as short communications. These have the same format requirements as full papers but are only up to 5 pages in length. Short Communications should not have subtitles such as Introduction, Materials and Methods, Results and Discussion - all these have to be merged into the running text. Short Communications preferably should have only 1-2 illustrations.

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