RESUL AND DISEUSSION

We have performed the chemical and microbiological testing of Granisetron material. It was observed that the prepared antiemetic formulation of granisetron injection is chemically stable in terms of potency of the drug product, it was observed that no impurities generation were observed.A formulation was prepared using the Granisetron and chemical stability was Performed as per ICH stability study guidance. It was observed that the developed formulation was stable at accelerated stability condition Temp and real-time condition for 6 Months. Granisetron Solubility study was studied using various parameters such as temperature and high speed stirring.

Selection and compatibility of preservative and chemical excipients were studied, The content of preservative was analyzed by chromatographic method (HPLC), developed formulation is multidose formulation hence Preservative efficacy study was performed.

Method of sterilization for anti emetic injection formulation was steam sterilization and filtration using 0.2 micron filter. Chemical Stability studies of multidose anti emetic injection formulation at accelerated and real-time conditions were performed. Chemical Analysis for assay (potency) was performed using the chromatographic method analysis using HPLC method. Assay found satisfactory it was observed that the formulation is stable for assay content. PH and particulate matter[84] [94] testing was performed.

Chemical parameters such as viscosity, Osmolality [85] [96]were studied. In Chemical stability thermal stress test was performed to determine the temperature and cooling shocks during storage of the formulation. It was observed that the formulation is chemically stable.

STABILITY REPORT
LAB SCALE BATCH
GRANISETRON INJECTION

Batch No. INJ/GRN/T-002 **Pack: 2 ml, clear glass Ampoules**

Sl. No.	*Tests*	*Specification*	Initial	Stability Condition								
				40°C±2°C/ 75%RH±5% RH						60°c		
				1 Week	2 Week	1Month	2Month	3 Month	6 Month	1 Week	2 Week	1 month
1	Appearance	Clear colorless liquid	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
2	Assay (%)	90-120	104.34	104.57	104.77	102.52	102.51	100.54	100.72	101.01	104.39	102.53
3	Preservative content (%)	80-120	101.37	101.98	ND	102.73	101.96	ND	ND	100.52	ND	102.79
4	pH	5.5-7.0	6.57	ND	6.27	6.53	ND	6.58	6.48	ND	6.35	6.41
5	Osmolality	For information only	251	ND	ND	245	ND	253	264	ND	266	282
6	Light Transmission	For information only	100.0	ND	ND	100.07	ND	100.64	100.83	ND	100.3	100.11
7	Color Value	For information only	-0.003	ND	ND	-0.001	ND	0.001	0.011	ND	-0.000	0.001
8	Single maximum imp.	--	2.10	2.11	2.10	3.93	1.56	1.91	8.0	2.02	2.10	4.03
	Total impurity	--	3.22	2.74	3.50	3.97	4.6	4.19	14.07	4.35	3.60	4.07

STABILITY REPORT
LAB SCALE BATCH
GRANISETRON INJECTION

Batch No. INJ/GRN/T-002 **Pack: 2 ml, clear glass Ampoules**

Sl. No.	*Tests*	*Specification*	Initial	Stability Condition*			
				30°C±2°C/ 65%RH±5% RH		25°C±2°C/ 60%RH±5% RH	
				3 Month	6 Month	3 Month	6 Month
1	Appearance	Clear colorless liquid	Complies	Complies	Complies	Complies	Complies
2	Assay (%)	90-120	104.34	100.24	100.04	100.35	100.68
3	Preservative content (%)	80-120	101.37	ND	ND	ND	ND
4	pH	5.5-7.0	6.57	6.55	6.44	6.49	6.41
5	Osmolality	For information only	251	249	254	247	251
6	Light Transmission	For information only	100.0	ND	100.59	ND	100.45
7	Color Value	For information only	-0.003	ND	0.008	ND	0.005
8	Single maximum imp.	--	2.10	1.94	3.9	1.98	2.06
	Total impurity	--	3.22	4.29	7.8	4.24	5.90

STABILITY REPORT
LAB SCALE BATCH
GRANISETRON INJECTION

Batch No. INJ/GRN/T-002 (Thermal cycling study) **Pack: 2 ml, clear glass Ampoules**

Sl. No.	Tests		Specification	Initial	After 3 Cycles
1	Appearance		Clear colorless liquid	Complies	Complies
2	Identification		90-120	Complies	Complies
3	pH		80-120	101.37	100.56
4	Assay (%)		5.5-7.0	6.57	6.60
5	Osmolality (mOsml/ Kg)		For information only	251	250
6	Light Transmission		For information only	100.0	100.0
7	Color Value		For information only	-0.003	-0.004
8	Single maximum imp.		--	2.10	2.11
9	Total impurity		--	3.22	3.25
10	Particulate Matter	≥10µ	Not more than 6000 particles per container	26	29
11		≥25µ	Not more than 600 particles per container	02	02

STABILITY REPORT
LAB SCALE BATCH
GRANISETRON INJECTION

Batch No. INJ/GRN/T-002 (Stress Testing study) **Pack: 2 ml, clear glass Ampoules**

Sl. No.	*Tests*	*Specification*	Initial	Stability Condition*		
				60°c		
				1 Week	2 Week	1 Month
1	Appearance	Clear colorless liquid	Complies	Complies	Complies	Complies
2	Assay (%)	90-120	104.34	102.01	102.96	101.80
3	pH	5.5-7.0	6.57	6.59	6.35	6.41
4	Osmolality	For information only	251	260	266	282
5	Light Transmission	For information only	100.0	100.00	100.3	100.11
6	Color Value	For information only	-0.003	-0.002	-0.000	0.001
7	Single maximum imp.	--	2.10	2.02	2.10	4.03
	Total impurity	--	3.22	4.35	3.60	4.07
8	Particulate Matter	≥10µ Not more than 6000 particles per container	26	28	30	40
		≥25µ Not more than 600 particles per container	02	01	05	10

STABILITY REPORT
LAB SCALE BATCH
GRANISETRON INJECTION

Batch No. INJ/GRN/T-002 (Particulate Matter) **Pack: 2 ml, clear glass Ampoules**

Sl. No.	*Tests*	*Specification*	Initial	Stability Condition								
				40°C±2°C/ 75%RH±5% RH						60°c		
				1 Week	2 Week	1 Month	2 Month	3 Month	6 Month	1 Week	2 Week	1 month
1	Particulate Matter	≥10µ Not more than 6000 particles per container	26	28	30	32	32	33	35	28	30	32
		≥25µ Not more than 600 particles per container	02	01	03	02	03	08	10	02	06	08

STABILITY REPORT
LAB SCALE BATCH
GRANISETRON INJECTION

Batch No. INJ/GRN/T-002 (Particulate Matter) **Pack: 2 ml, clear glass Ampoules**

Sl. No.	*Tests*	*Specification*	Initial	Stability Condition*			
				30°C±2°C/ 65%RH±5% RH		25°C±2°C/ 60%RH±5% RH	
				3 Month	6 Month	3 Month	6 Month
1	Particulate Matter	≥10µ Not more than 6000 particles per container	26	35	38	32	35
		≥25µ Not more than 600 particles per container	02	07	09	08	10

Table No. 01: Viscosity findings of Granisetron Injection, With Preservative (1.0 mg/mL)

Sr. No.	% Torque	rpm	Temperature (^{0}C)	Viscosity (cP)
1	2.9	100	27.8	0.87
2	5.1	150	27.8	1.00
3	6.0	180	27.8	1.02
4	7.4	200	27.8	1.11

Table No. 01: Viscosity findings of Granisetron Injection, Preservative Free (0.1 mg/mL)

Sr. No.	% Torque	rpm	Temperature (^{0}C)	Viscosity (cP)
1	2.5	100	27.8	0.75
2	4.9	150	27.8	0.98
3	6.0	180	27.8	1.00
4	7.2	200	27.8	1.08

From the results it was observed that as the shear stress increases (% torque) there is a gradual isncrease in the shear rate (rpm). Moreover, the viscosity of Granisetron Injection, With Preservative (1.0 mg/mL) and Preservative Free (0.1 mg/mL) goes on increasing as the % torque and rotational speed of the spindle increases.

The graphs were plotted to study the effect of % torque and the effect of increasing spindle speeds (rpm) on the viscosity of Granisetron Injection.

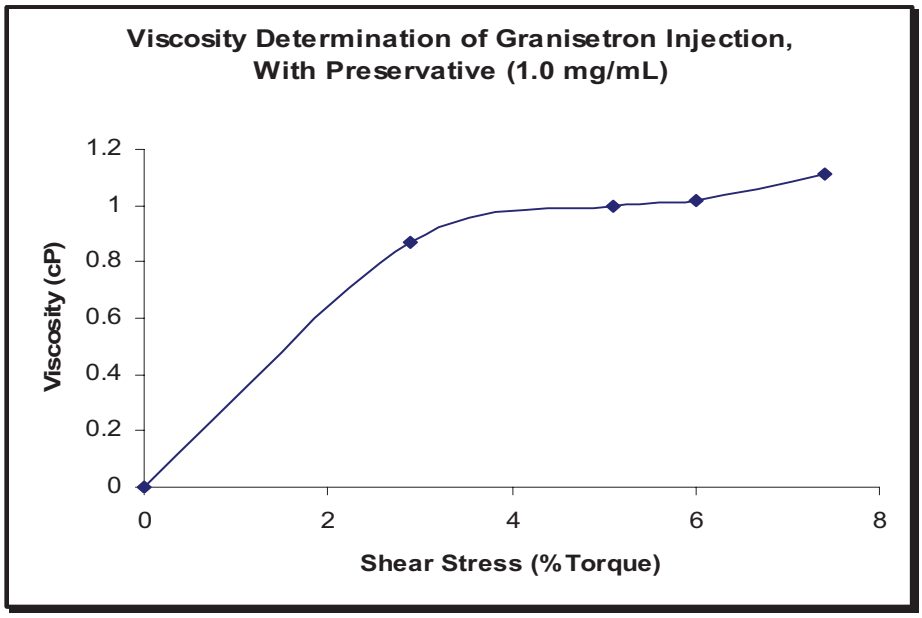

Figure No. 1: Graphical representation of Shear stress (% Torque) Vs Viscosity (cP) for Granisetron Injection, With Preservative (1.0 mg/mL)

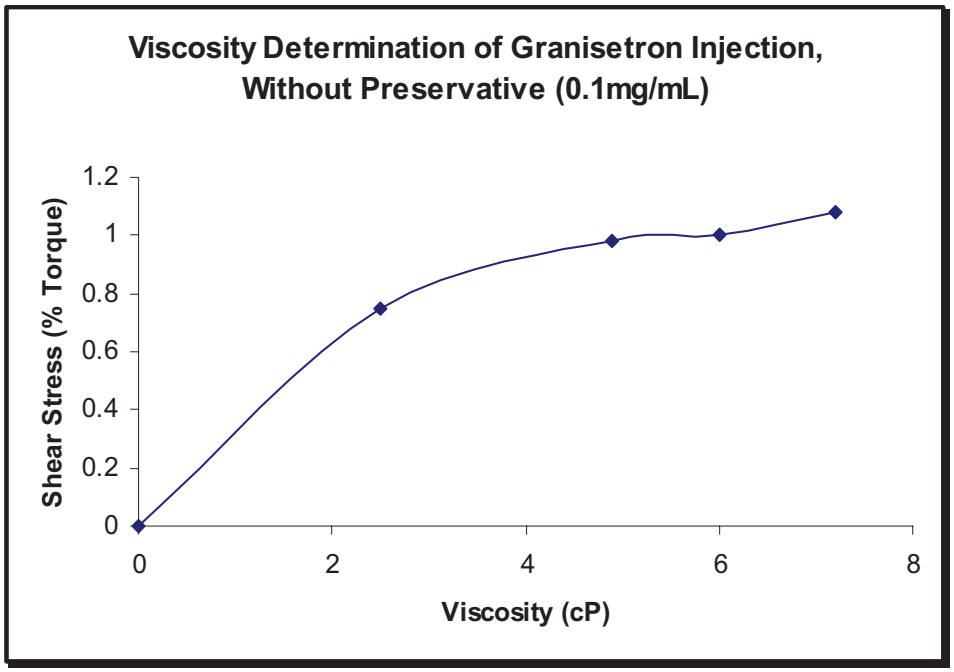

Figure No. 2: Graphical representation of Shear stress (% Torque) Vs Viscosity (cP) for Granisetron Injection, Preservative Free (0.1 mg/mL)

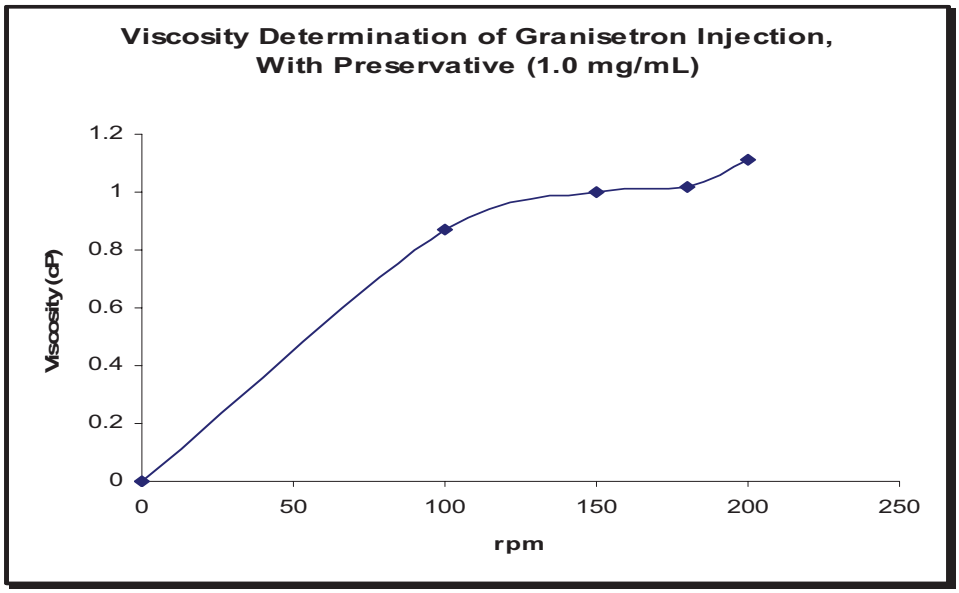

Figure No. 3: Graphical representation of rpm Vs Viscosity (cP) for Granisetron Injection, With Preservative (1.0 mg/mL)

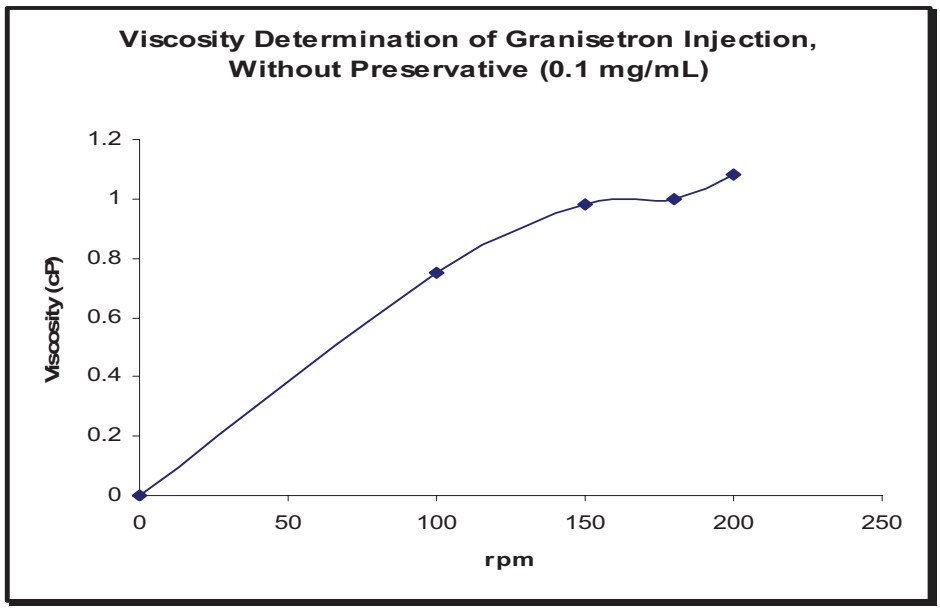

Figure No. 4: Graphical representation of rpm Vs Viscosity (cP) for Granisetron Injection, Preservative Free (0.1 mg/mL)

Conclusion:

From the results and the above graphs, it was concluded that the Granisetron Injection (1.0mg/mL) and Granisetron Injection (0.1 mg/mL) has the comparable viscosity values when studied at different parameters like % torque and rpm. The viscosity values of formulated Granisetron Injection are very less, which ensures that the less force is required for its administration and hence ease of administration.

STERILITY TEST REPORT

Product : Granisetron Hcl. Injection Batch No:INJ/GRN/T-002

Date of testing :30/10/08 Date of completion:13/11/08Method of test : Membrane filtration**Media used:** FTGM – Fluid thiglycollate medium 100ml

SCDM – Soyabean casein medium 100ml

B. No./Lot. No. of Membrane	F8AN245NH03
Mfg. Dt. of Membrane	NA
Exp. Dt. of Membrane	June 10
Type of membrane used	Mixed esters of cellulose
Pore size of membrane	0.45 µ
No. of samples	20 No.
Quantity of samples used	100 mL

OBSERVATION FOR SAMPLE (Initial)

MEDIA	DAY													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCDM	-	-	H	-	-	-	-	-	-	H	-	-	-	-
FTGM	-	-	H	-	-	-	-	-	-	H	-	-	-	-

OBSERVATION FOR POSITIVE CONTROL AND NEGATIVE CONTROL

MEDIA	Organism used	DAY													
		1	2	3	4	5	6	7	8	9	10	11	12	13	14
SCDM	C.Albicans	-	-	+											
	- ve control	-	-	H	-	-	-	-	-	-	H	-	-	-	-
FTGM	Cl.Sporogenes	-	+												
	- ve control	-	-	H	-	-	-	-	-	-	H	-	-	-	-

'+' = GROWTH '-' = NO GROWTH

Remarks: Evidence of microbial growth is not found. The sample complies with test for sterility.

Discussion

We have performed the chemical and microbiological testing of Granisetron material it was observed that the prepared antiemetic formulation of granisetron injection is chemically stable in terms of potency of the drug product, it was observed that no impurities were generated during the stability studies of the formulated produt.

A formulation was prepared using the Granisetron and chemical stability was performed as per ICH stability study guidance. It was seen the formulated product is quite stable at stress and accelerated condition stability.

It was observed that the developed formulation was stable at accelerated stability condition temp and real-time condition for 6 Months. Therefore we can conclude that the developed formulation is stable at room temp condition for the period of 24 months i.e., the expiry of the developed formulation is 24 months, further studies after the end of shelf life can be performed to increase the expiry of the drug product.

Granisetron Solubility was studied using various parameters such as temperature and high speed stirring. It was observed that the granisetron is easily soluble in water and therefore as product vechile water is suitable for the drug product preparation.

Selection and Compatibility of chemical excipients were studied. It was observed that the selected materials are compatible to each other and no incompatibility issue was observed.

Selection and compatibility of preservative was studied, and the content of preservative was analyzed by chromatographic method (HPLC), developed formulation is multidose formulation hence preservative efficacy study was performed. It was concluded that the concentration of benzyl alcohol is capable to reduce the microbial growth.

Method of sterilization for anti emetic injection formulation was the steam sterilization and filtration using 0.2 micron filter. By performing the sterility study it was concluded that the product filtration is the suitable method for the sterilization of drug product of granisetron .

Chemical Stability studies of multidose anti emetic injection formulation at accelerated and real-time conditions were performed. Chemical Analysis for assay (potency) was performed using the chromatographic method analysis using HPLC method. Assay was found satisfactory. It was observed that the formulation is stable for assay content. PH and particulate matter testing was performed.

Chemical parameters such as viscosity, Osmolality were studied.

In Chemical stability thermal stress test was performed to determine the temperature and cooling shocks during storage of the formulation. It was observed that the formulation is chemically stable. we can conclde that the prepared formulation is chemically stable .