Journal of Advanced Zoology
ISSN: 0253-7214
Volume 45 Issue S-1 `Year 2024 Page 48:54

Formulation And Evaluation Of Mouth Dissolving Tablets Of Amoxapine

G. Bhagya Buela[1*], Shaheen[2], S. Suguna[3] Nandhini. M[4] & Voleti Vijaya Kumar[5]

[1,2,3] Shadan women s college of pharmacy, Khairtabad, Hyderabad, Telangana, India.*
[4,5] School of Pharmacy, Sathyabama Institute of Science and Technology, Chennai, Tamil Nadu, India.

***Corresponding Author:-** G.Bhagya Buela*
**Associate professor Shadan women s college of pharmacy Khairthabad , Hyderabad. PIN 500004*
Email:- gudipalli.buela@gmail.com 8008006438

Abstract

The objective of the present study is to design and formulate orodispersible tablets of Amoxapine using novel Co-processed superdisintegrants by employing direct compression method. Amoxapine is used to treat symptoms of depression. Amoxapine is a class II drug with high permeability and low solubility. There is a need to develop a formulation of Amoxapine that will enhance the bioavailability of the drug by decreasing the disintegration time. Thus improves patient compliance generate rapid response enhances bioavailability and also reduces dose of drug. In this study ODTs are prepared by direct compression method using novel super disintigrants in different proportions .The powder blend is subjected to pre compression parameters including bulk density, true density, tapped density, cars index, Hausner's ratio and angle of repose. The formulations are evaluated for weight variation, hardness, wetting time, water absorption test, disintegration time and in vitro dissolution studies and all formulations complies its Pharmacopoeial standards. The tablets are evaluated and the results compared for all four super disintigrants revealed cross povidone to be the most efficious super disintigrants to formulate mouth dissolving tablets of Naproxen sodium as suggested by the dispersion time , disintegration time and drug dissolution profiles.

Keywords: ***Amoxapine, Ludipress, Star Lac, Pearlitol SD and Oral Disintigrating tablets***

INTRODUCTION:

Orodispersible tablets are the promising dosage forms for better patient compliance especially for patients, while travelling and when there is a difficulty in swallowing the dosage form for pediatrics and geriatrics. Keeping in mind all the above factors, the aim was set to formulate and evaluate orodispersible tablets of Amoxapine using co-processing superdisintegrants to obtain a product with added value related to the ratio of its functionality/price. Amoxapine is a weak acidic drug; hence it remains in partially non ionized form at oral P^H which favors pregastric absorption. These parameters make the drug ideal candidate for ODT. These tablets display a fast and spontaneous de-aggregation in the mouth, soon after the contact with saliva. The active agent can thus rapidly dissolve in the saliva and be absorbed through whatever membrane it

encounters, during deglutition, unless it is protected from pre-gastric absorption. To fulfill these requirements, tablets must be highly porous, incorporating hydrophilic excipients, able to rapidly absorb water for a rapid deaggregation of the matrix. Different technological techniques, such as freeze drying or moulding or direct compression are currently employed to prepare the formulations of this type present on the pharmaceutical market.

Conventional dosage form of Amoxapine tablets gains less advantageous due to bad taste and high first pass metabolism resulting in non compliance and ineffective therapy. The basic approach used in the development of ODT is the use of novel co super disintigrants for design ODT. Thus the objective of present study is to develop ODT's of amoxapine and pregastric absorption avoids, first pass effect and gastric discomfort. It has good solubility in water and saliva and inherent ability to permeate through oral mucosal tissue. The drug moiety is a weekly acidic drug, so remains in partially non ionized form at oral cavity's pH, which favors its pregastric absorption. So, all the mentioned parameters make the drug ideal candidate for design of ODTs with regards to patient compliance by minimizing its side effects and rapidifying the action.

EXPERIMENTAL:

Materials:

Amoxapine and super disintigrants were obtained as gift samples from Signet Chemical Corporation Pvt. Ltd. Mumbai. Talc and magnesium stearate used for the preparation of tablets were of Pharmacopoeial grade.

METHODS

Evaluation of flow properties of blend

The quality of tablet is generally dictated by the quality of physicochemical properties of blends. There are many formulation and process variables involved in mixing step and all these can affect the characteristics of blends produced. Micromeretic properties like bulk density, true density, Carr's index, Hausner's ratio and Angle of repose. Authentication of drug and drug excipient compatibility are carried out by IR & UV analysis.

Preparation of the tablet formulations by direct compression method

All the ingredients such as Amoxapine, Novel Co superdisintegrants were weighed and passed through #60 mesh separately. Then the ingredients were mixed and compressed into tablet using 7mm flat faced punches on 16 station rotary tablet machine. Formulations of Amoxapine by direct compression method are shown in Table 1.

Evaluation of Formulated tablet

1. **Hardness:** Compression forces required to break the tablet was measured.

2. **Weight variation test**

20 tablets were randomly selected from each formulation trial batch and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight of 20 tablets.

3. **Friability**

Roche fribalator was used to determine the friability. Pre weighed tablets are placed in Roche Fribalator and rotated at a speed of 25 rpm per minute or upto100 revolutions.

4. **Disintegration time**:

Disintegration time is the time taken by the tablet to breakup into smaller particles. The disintegration test is carried out in an apparatus containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 times per minute in a medium of 900 ml saliva buffer pH 6.8 which is maintained at 37 ± 2^0C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (# 10) was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30s.

5. In Vitro Dispersion Time: One tablet was placed in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37±0.5ºC and the time required for complete dispersion was determined .

6. Fitness of dispersion: this test was performed by placing 2 tablets in 100ml of water and stir it gently till the tablets gets completely dispersed. The formulation is considered to form a smooth dispersion if it passes through the sieve of nominal mesh 710microns without leaving residue on the mesh.

7. Wetting Time[5,6]: Twice folded tissue paper was placed in a petri-dish having an internal diameter of 5 cm containing 6 ml of water. A tablet having a small amount of rosalin powder on upper surface was placed on tissue paper. The time required to develop red color on upper surface of the paper was considered as the wetting time.

8. Water Absorption Ratio (R)[7]: The weight of the tablet prior to placement in the petri-dish was noted utilizing a digital balance (ELB 300). The wetted tablet was removed and reweighed. Water absorption ratio (R) was then determined according to the following equation:

$$\% R = \frac{w_a - w_b}{w_b} x100$$

Where, w_a and w_b were tablet weights before and after water absorption respectively.

9. Dissolution studies[8]: Dissolution is a process by which the disintegrated solid solute enters the solution. The test determines the time required for a definite percentage of the drug in a tablet to dissolve under specified conditions.
In vitro dissolution studies of the optimized fast dissolving tablets of Amoxapine was performed using USP type II paddle apparatus. One tablet was used in each test. Aliquots of the dissolution medium (5 ml) were withdrawn at specific time intervals (5, 10, 15, 20,30min.) and replaced immediately with equal volume of fresh medium. The samples were filtered through 0.22µm membrane filter disc and analyzed for drug content by measuring the absorbance at 294 nm. Drug concentration was calculated from the standard calibration curve and expressed as cumulative percent drug dissolved. The release studies were performed in replicates of six.

Dissolution Parameters
Dissolution Apparatus : USP Apparatus Type II (Paddle)
Dissolution Medium : 6.8
Volume : 900 ml
Temperature : 37±2° C
Rpm : 50
Sampling Intervals (min): 5, 10, 15, 20 and 30 min
Specification: NLT 80% (Q) of the labelled amounts of Amoxapine.

10. Drug Content Uniformity: For the content uniformity test, ten tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 25 mg of Amoxapine was extracted into methanol and liquid was filtered (0.22µm membrane filter disc (Millipore Corporation). The drug content was determined by measuring the absorbance at 294 nm (using UV-vis spectrophotometer, Shimadzu 1700) after appropriate dilution with methanol. The drug content was determined using standard calibration curve. The mean percent drug content was calculated as an average of six determinations.

RESULTS AND DISCUSSION

Fifteen formulations were prepared for orodispersible tablets of Amoxapine by direct compression method employing co-processed superdisintegrants. The direct compression blends were evaluated for the flow properties and were found to have good flow properties according to the limits. The bulk density of the blends with co-processed superdisintegrants were found to be in the range of 0.39±0.04 to 0.69±0.02 g/cm^3 and the tapped density in the range 0.45±0.03 to 0.80±0.03g/cm^3.The compressibility index of various blends was found to be in the range 11.29±0.02 to 13.75±0.05and the Hausner's ratio 1.134±0.02-1.16±0.02. The angle of repose of various powder blends, prepared with different co-processed superdisintegrants was calculated. It was found to be in the range 26.3±0.08to 30.0±0.07. Tablets were evaluated by using Pfizer Hardness tester. Hardness of the tablets was found in the range of 2.98±0.02 to 3.15±0.05 kp. Uniform hardness was obtained due to equal compression force. The percentage weight variations for all formulations

were done. All the formulated tablets passed weight variation test as the percent weight variation was within Formulation the pharmacopoeial limits as the formulation blend of all the formulations have a good flow thus the percent weight deviation was in between 5% of the average weight. The values of friability test were in the range from 0.58±0.05 to 0.81±0.04 %. The percent friability of all the formulation was less than 1% ensuring that the tablets were mechanically stable. Tablets were evaluated by using assay method. The drug content was found to be in the range 98.15±0.5 to 100.12±0.2%w/w. Wetting time is closely related to the inner structure of the tablet and hydrophilicity of its excipients. Out of all the formulations, StarLac containing formulations F6, F7, F8, F9, F10 showed less wetting time of 52±0.12, 48±0.1, 42±0.5, 33±0.6, &25±0.4 respectively and its disintegration action is by rapid wicking, swelling followed by disintegration. In all formulations it was observed that wetting time decreased with increase in the concentration of co-processed superdisintegrants. Water absorption ratio, which is an important criterion for understanding the capacity of disintigrants to swell in presence of little amount of water was calculated. It was found to be in the range of 42±0.08 to 77±0.12.The water absorption ratio increased with increase in the concentration of co-processed superdisintegrants from 1-5%. This increase was due to the water up-taking ability of the superdisintegrants. More the co-processed superdisintegrant concentration, greater was the water uptake and hence, an increase in water absorption. The *in vitro* dissolution study for all formulations was studied in phosphate buffer pH 6.8 using tablet dissolution tester USP XXIII apparatus II. The predetermined samples were withdrawn at different time intervals and analyzed at 294 nm. Cumulative drug release was calculated on the basis of the mean amount of Amoxapine present in the respective tablet. The dissolution rate was found to increase linearly with increase in the concentration of superdisintegrant. Formulations F1, F2, F3, F4& F5 which contained Ludipress 1%, 2%, 3%, 4% and 5%w/w respectively, showed drug release of 45.23±0.7, 61.23±0.1,75.54±0.1,85.52±0.4,93.58±0.1% .Formulations F6, F7, F8, F9 & F10 which contained StarLac1%, 2%, 3%, 4% and 5%w/w respectively, showed drug release of 48.01±0.3, 63.02±0.1,72.23±0.4,79.00±0.1,98.95±0.7%were shown in table no 6.7 and Formulations F11, F12, F13, F14 & F15 which contained Pearlitol1%, 2%, 3%, 4% and 5%w/w respectively, showed drug release of 46.21±0.1, 59.32±0.9,72.69±0.4,87.59±0.5,92.54±0.1%.

CONCLUSION:

In the current study a successful attempt was made to formulate Orodispersable tablets of Amoxapine by direct compression method using co-processed superdisintegrants like Ludipress, StarLac, & Pearlitol.
The flow characters and the compression parameters of all the formulations were found to be within the limits.
The tablets showed good water absorption ratios. The disintegration time for the optimized formula was found to be 21 sec. The dispersion time and wetting time were also within the limits.
98.95%w/v drug was released into the dissolution medium within 30 min. From the dissolution profiles, the mechanism of drug release followed First order kinetics. The stability studies showed that the tablets were stable without microbial contamination, limited amount of water uptake. The dissolution data indicated that there is no change in the drug release pattern and the drug content during the stability study was in the range of 98.95±0.7 to 98.97±0.3 %w/w.
The studies indicated that the tablets containing 5%w/w of formulation F10 containing StarLac as co-processed superdisintegrant by direct compression technique was found to be the best formulation.

REFERENCES:

1. Md. Armin Minhaz, enhancement of solubility and dissolution properties of Amoxapine by solid dispersions, International Journal of pharmacy and lifesciences march 2012, vol-3, issue-3, Pg. No:1510-1518..
2. Lachman, L, Lieberman, H. A., Kanig, J. L., The Theory and Practice of Industrial Pharmacy, 3rd edition, Varghese Publishing House, Bombay, 297, 1987.
3. Shaikh S et al., Formulation and evaluation of orodispersible tablets of piroxicam. Journal of Pharmaceutics and Cosmetology. 2010;1(2): 2-8.
4. Lalla JK, Mamania HM. Fast dissolving rofecoxib tablets. Indian Journal of Pharmaceutical Sciences 2004; 59(4):23-26.
5. Shaikh S et al, Formulation and evaluation of orodispersible tablets of piroxicam. Journal of Pharmaceutics and Cosmetology2010;1(2): 2-8.

6. Panigrahi R., Behera S., A Review On Fast Dissolving Tablets., Webmed Central Quality and patient safety WMC00809 2010;1(3): 1-15.
7. Mahaveer Pr. Khinchi., Orally disintegrating tablets: A future prospectus, Int J Pharm Sci Bio 2012;3(4):71-79.
8. US Food and Drug Administration, Drug database, Dissolution methods, www.accessdata.fda.gov.25/7/2007.
9. Formulation And Evaluation Of Mouth Dissolving Tablets Of Escitalopram Oxalate Using Natural Superdisintegrants jm kumar, vv kumar, v gunasekharan - inventi rapid: novel excipients, 2013

Table no 1: Flow properties of the blend

Formula	Bulk density (kg/cm^3)	Tapped density (kg/cm^3)	Compressibility index (I)	Hausner's ratio	Angle of repose(θ)
F1	0.39±0.04	0.45±0.03	13.33±0.04	1.15±0.05	27.6±0.03
F2	0.42±0.02	0.48±0.00	12.5±0.04	1.14±0.03	28.4±0.02
F3	0.44±0.03	0.50±0.02	12.0±0.06	1.14±0.02	26.3±0.08
F4	0.46±0.05	0.52±0.05	11.53±0.01	1.13±0.04	30.0±0.07
F5	0.50±0.05	0.57±0.02	12.28±0.05	1.14±0.07	26.8±0.3
F6	0.44±0.03	0.50±0.21	12.00±0.02	1.14±0.06	29.3±0.5
F7	0.51±0.02	0.58±0.05	12.06±0.05	1.14±0.02	29.7±0.10
F8	0.54±0.01	0.61±0.01	11.47±0.04	1.13±0.05	27.5±0.08
F9	0.55±0.21	0.62±0.08	11.29±0.02	1.13±0.08	28.4±0.05
F10	0.57±0.00	0.66±0.07	13.63±0.09	1.16±0.02	29.2±0.01
F11	0.58±0.02	0.66±0.03	12.21±0.05	1.14±0.02	26.7±0.02
F12	0.60±0.02	0.68±0.06	11.76±0.05	1.13±0.02	28.5±0.01
F13	0.65±0.02	0.735±0.07	11.56±0.05	1.13±0.02	29.5±0.08
F14	0.68±0.02	0.78±0.03	12.82±0.05	1.15±0.02	29.9±0.04
F15	0.69±0.02	0.80±0.03	13.75±0.05	1.16±0.02	28.9±0.03

*****All the values are expressed as mean ±Standard deviation; n=3

Table no 2: Evaluation of physical properties of tablets

FORMULA	THICKNESS (mm)	HARDNESS (Kg/cm^2)	AVERAGE WEIGHT (mg)	% FRIABILITY	ASSAY
F1	2.93±0.02	3.02±0.02	100.5±0.01	0.62±0.02	98.15±0.5
F2	2.94±0.04	2.99±0.05	100.2±0.02	0.81±0.04	99.85±0.4
F3	2.98±0.05	2.98±0.02	100.7±0.08	0.71±0.08	98.32±0.2
F4	2.99±0.02	3.1±0.06	99.2±0.09	0.65±0.01	99.65±0.6
F5	2.99±0.07	3.15±0.05	100.1±0.06	0.61±0.05	99.95±0.7
F6	2.95±0.02	2.98±0.04	100.8±0.02	0.59±0.01	99.15±0.5
F7	2.99±0.05	2.99±0.01	99.03±0.05	0.6±0.02	100.12±0.2
F8	2.96±0.01	3.09±0.05	99.80±0.03	0.58±0.05	98.99±0.3
F9	3.0±0.04	3.13±0.06	100.15±0.05	0.62±0.05	99.11±0.2
F10	3.0±0.03	3.08±0.02	100.1±0.03	0.59±0.002	100.05±0.3
F11	2.96±0.02	3.10±0.06	99.8±0.02	0.711±0.04	98.99±0.25
F12	2.98±0.04	3.09±0.03	99.8±0.04	0.721±0.05	98.69±0.25
F13	3.02±0.03	3.10±0.05	98.8±0.06	0.73±0.01	98.19±0.21
F14	2.98±0.02	3.14±0.03	99.3±0.01	0.75±0.02	99.59±0.03
F15	3.05±0.01	3.13±0.01	99.1±0.04	0.71±0.04	98.18±0.21

All the values are expressed as mean ±Standard deviation; n=6

Table no 3: Evaluation of wetting time, *In-vitro* dispersion time, fitness of dispersion, disintegration time&water absorption ratio

Formulation code	Wetting time (sec.)	*In-vitro* dispersion time ('min, "sec)	Fitness of dispersion	Disintegration time(sec)	Water absorption ratio
F1	62±0.2	3'05" ±28"	Failed	42±2	63±0.1
F2	55±0.12	2'30" ±30"	Failed	39±2	64±0.15
F3	41±0.3	2'10" ±25"	Failed	32±2	66±0.07

F4	36±0.4	2'55" ±10"	Failed	30±2	69±0.03
F5	31±0.21	2'01" ±20"	Passed	28±2	42±0.08
F6	52±0.12	3'01" ±30"	Failed	35±2	45±0.17
F7	48±0.1	2'50" ±22"	Failed	33±2	49±0.16
F8	42±0.5	2'28" ±15"	Failed	30±2	52±0.15
F9	33±0.6	2'10" ±11"	Passed	26±2	55±0.16
F10	25±0.4	1'01" ±12"	Passed	21±2	58±0.10
F11	59±0.06	4'16" ±23"	Failed	40±2	63±0.09
F12	51±0.1	3'58" ±20"	Failed	32±2	65±0.10
F13	48±0.15	3'45" ±09"	Passed	30±2	69±0.12
F14	44±0.11	3'18" ±01"	Failed	27±2	75±0.17
F15	38±0.22	2'59" ±10"	Passed	26±2	77±0.12

All the values are expressed as mean ±Standard deviation; n=6

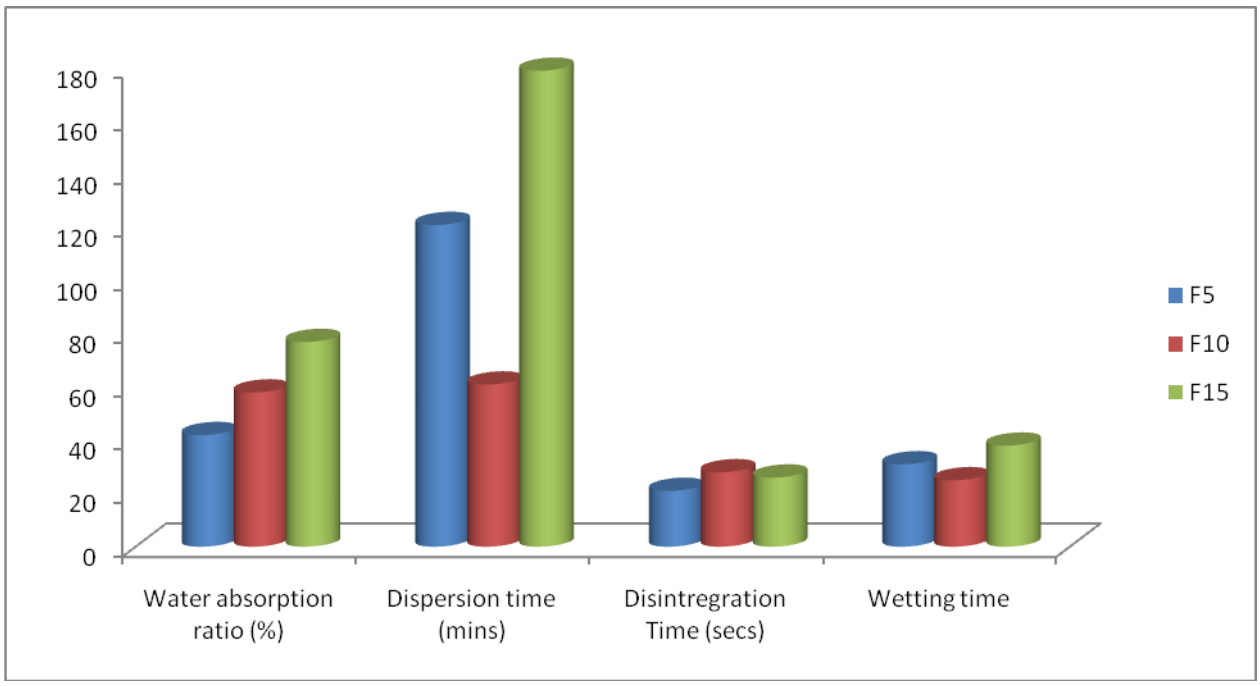

Figure 1: Comparison of Water absorption ratio, Dispersion time, Disintegration time & Wetting time of the tablets

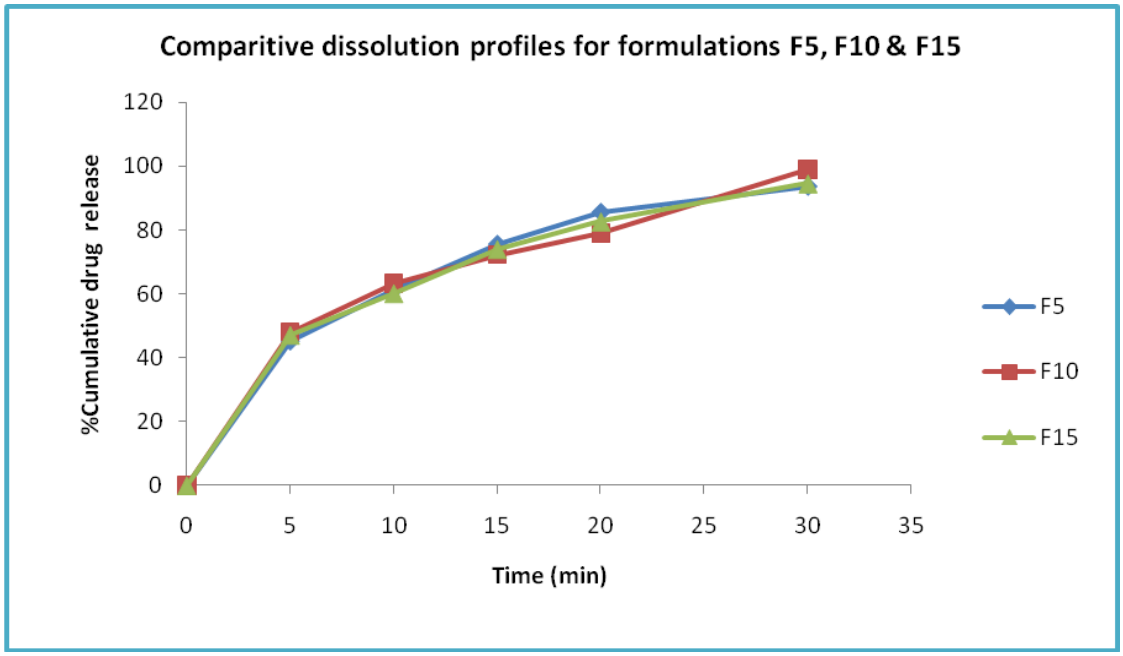

Figure 2: Comparative dissolution profiles for F5, F10, F15 formulations

Table no 4: Kinetic Studies

Formula	Correlation coefficient			Release rate			
	Zero order	First order	K_0	K_1	T_{25}	T_{50}	T_{90}
F1	0.8935	0.9767	3.257	0.061	3.729	10.337	36.565
F2	0.8959	0.9815	3.377	0.067	3.500	9.566	33.643
F3	0.8976	0.9902	3.622	0.080	3.118	8.197	28.355
F4	0.9018	0.9930	3.689	0.083	3.073	7.934	27.229
F5	0.9073	0.9966	3.933	0.098	2.737	6.895	23.399
F6	0.8977	0.9838	3.400	0.068	3.527	9.475	33.087
F7	0.9030	0.9822	3.498	0.072	3.294	8.954	31.421
F8	0.9017	0.9873	3.770	0.087	2.910	7.587	26.152
F9	0.9076	0.9911	3.913	0.095	2.720	6.988	23.931
F10	0.9182	0.9859	3.941	0.095	2.658	6.939	23.934
F11	0.8823	0.779	3.326	0.066	3.546	9.716	34.206
F12	0.9036	0.9827	3.463	0.070	3.369	9.159	32.144
F13	0.8915	0.9864	3.676	0.083	3.003	7.896	27.314
F14	0.9072	0.9928	3.905	0.095	2.768	7.042	24.010
F15	0.9113	0.9927	3.903	0.094	2.725	7.027	24.102