WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 5, 1751-1759. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF FAST DISSOLVING FILMS OF ENALAPRIL MALEATE.

Harshada Deoghare*, Prajakta Ahire, Ghanashyam Yadav and Avish Maru

Department of Pharmaceutics, Loknete Dr. J. D. Pawar College of Pharmacy Manur, Tal. Kalwan, Dist. Nashik.

Article Received on
19 March 2016,

Revised on 09 April 2016,
Accepted on 29 April 2016

DOI: 10.20959/wjpr20165-6243

***Corresponding Author**
Harshada Deoghare
Department of Pharmaceutics, Loknete Dr. J. D. Pawar College of Pharmacy Manur, Tal. Kalwan, Dist. Nashik.

ABSTRACT

Enalapril Maleate is an angiotensin converting enzyme (ACE) inhibitor, used mainly in the treatment of hypertension and angina pectoris. It shows low bioavailability 40-60% due to high hepatic first pass metabolism. Hence the present study investigated the possibility of developing Enalapril Maleate fast dissolving sublingual films allowing fast, reproducible drug dissolution in the oral cavity, thus by passing first pass metabolism to provide rapid onset of action of the drug. The fast dissolving films were prepared by solvent casting method. Hydroxylpropyl methylcellulose (HPMC K 15) and polyvinyl alcohol were used in combination as film forming polymer, due to their hydrophilic nature and palatable taste. To decrease the disintegration time of formulations sodium starch glycolate was used as disintegrating agent. Glycerin is used as a cooling agent, sodium lauryl sulphate is used as a oral penetration enhancer and mannitol, aspartame is used as sweetening agent. All the films formulations (F1-F9) was evaluated for their thickness, weight variations, tensile strength, percentage elongation, folding endurance, surface pH, in-vitro disintegration, drug content, in-vitro drug release and ex-vivo permeation. Disintegration time showed by the formulations was found to be in range of 20-40 sec. Formulations F2 showed 90% drug release within 15 min. The film showed an excellent stability at least for 4 weeks when stored at 40^0C and 75% in humidity.

KEYWORDS: Enalapril Maleate, Fast Dissolving Films, Mouth Dissolving Films.

INTRODUCTION

Fast dissolving drug-delivery system (FDDS) was an advancement that came into existence in the early 1970s and combats the use of the tablets, capsules and syrups, which are the other

oral drug-delivery systems. These delivery systems serve a major benefit over the conventional dosage forms because the drug gets disintegrated rapidly and dissolves in the saliva without the use of water. Inspite of the downside that is, a lack of immediate onset of action, these oral dosage forms have beneficial purposes such as accurate dosing, self-medication, increased patient compliance, ease of manufacturing and lack of pain. The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy and ease of administration.

Fast dissolving film is a type of drug delivery system, which when placed in the oral cavity it rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption, without chewing and intake of water. These films have a potential to deliver the drug systemically through intragastric, sublingual or buccal route of administration and also has been used for local action. This type of technology offer a convenient way of dosing medication, not to special population groups like pediatric, geriatric, bedridden patients, mentally ill patients, but also to the general population As the fast-dissolving film is taken through the sublingual route, rapid absorption of drug is possible, which finally leads to quick onset of drug action and prevent the first pass-metabolism of the drug.

Enalapril maleate is an angiotensin converting enzyme (ACE) inhibitor, used mainly in the treatment of hypertension, congestive heart failure and angina pectoris. Enalapril maleate is a BCS class 1 drug. It has a metallic taste. Its onset of action is quick. It has low bioavailability (40-60%) due to hepatic first pass metabolism. Hence to improve its therapeutic efficacy and bioavailability the drug may be administered by oral route through films. Fast dissolving drug delivery of enalapril maleate may circumvent hepatic first pass metabolism and improve bioavailability. Hence the present work deals with the formulation and characterization of Fast dissolving film of enalapril maleate using Film forming polymer hydroxyl propyl methyl cellulose K15 (HPMC K15) and polyvinyl Polyvinyl Alcohol.

MATERIALS AND METHODS

Materials

Enalapril Maleate was received as a gift sample from Flamingo Pharmaceutical Ltd, Rabale, New Mumbai. HPMC K15, PVA and other ingredients were procured from balaji drug supplier. Chemicals used in this study were of analytical grade.

Methods

Preparation of fast dissolving film

Films were prepared by solvent casting method. Polymer was weighed accurately and dissolved in water and add glycerine in this solution (solution I). In another beaker the drug and other ingredient dissolve in water (solution II) and mix both this solution (solution I and II) with the help of magnetic stirrer. The colour and flavour add in the mixture and stir continuously for 15 min. kept for 1hour to remove all the air bubbles entrapped. Then transfer the solution in petridish and allowed to dry at room temperature for 24 hrs. After drying, these films were removed from the petridish and cut into definite shapes and size. For further evaluation films are packed in aluminum foil and placed in desiccators.

Table No. 1: Composition of Enalapril Maleate fast dissolving films.

Formulation	Enalapril Maleate (mg)	HPMCK15 (mg)	PVA (mg)	GLY (mg)	SSG (mg)	SLS (mg)	ASP (mg)	Col. (ml)	Flv. (ml)	WATER UPTO (ml)
F1	10	40	10	5	3	1.5	5	QS	QS	QS
F2	10	40	15	5	3	1.5	5	QS	QS	QS
F3	10	40	20	5	3	1.5	5	QS	QS	QS
F4	10	45	10	5	3	1.5	5	QS	QS	QS
F5	10	45	15	10	3	1.5	5	QS	QS	QS
F6	10	45	20	10	3	1.5	5	QS	QS	QS
F7	10	50	10	10	3	1.5	5	QS	QS	QS
F8	10	50	15	10	3	1.5	5	QS	QS	QS
F9	10	50	20	10	3	1.5	5	QS	QS	QS

Evaluation of Enalapril Maleate Films

Appearance, Shape and Thickness

The formulated films of Enalapril Maleate were checked for their appearance, shape and thickness. The thickness of randomly selected 5 test films was determined at five different places using a micrometer and mean value was calculated.

Weight variation

Weight variation test was performed by taking weight of five films of every formulation individually and then average weight was calculated.

Surface pH

The surface pH of films was determined by placing film in petridish and moistened with few drops of distilled water and allowed to moisten for 1 hrs. After that bring an electrode of pH meter in contact with surface of film and pH were noted.

Folding endurance

It was determined by repeatedly folding one film at the same place till it broke. The number of times that film can be folded at the same place without breaking gives the value of the folding endurance.

Drug content estimation

The film (area =2×2 cm2) was placed in beaker and to this add sufficient volume of phosphate buffer pH 6.8 and dissolved the film with help of magnetic stirrer. Filter this solution and transferred into 100 ml volumetric flask. Make up final volume (i.e. 100ml) with remaining phosphate buffer pH 6.8 solutions. The absorbance of solution was measured at ʎ ؤmax 213 nm with help of UV spectrophotometer (LABINDIA 3000+ UV –VIS spectrophotometer). The experiment was performed in triplicate.

Disintegration time

In vitro disintegration time was determined by placing the film (area =2×2 cm2) in beaker containing 10ml of phosphate buffer and swirling at interval of 5sec. the time at which films start to disintegrate considered as disintegration time.

In-vitro drug release studies

The In-vitro drug dissolution study was carried out using USP dissolution test apparatus (USP type-II) at temperature 37+ 0.5°C and 50 rpm. The phosphate buffer pH6.8 (300ml) was used as the media. During the study 5ml of test sample was withdraw at 15sec intervals and the absorbance of sample taken at ʎ max 213nm with help of UV spectrophotometer (LABINDIA 3000+ UV –VIS spectrophotometer). The values were transformed into concentration using standard calibration curve. All data obtained are summarized in table No.3.

RESULTS AND DISCUSSION

Enalapril Maleate fast dissolving films were prepared and evaluated for Appearance, Size, Shape and Thickness, Surface pH, Weight uniformity, folding endurance, drug content, Disintegration and dissolution. All the films were transparent, the thickness was varies between 0.12±0.004mm to 0.25±0.005mm. The formulation (F2) shows thickness values 0.18±0.004mm there was no more significant difference in SD. The weight of films (F1-F9) was found to be in range of 50±0.540 to 62±0.577, the weight of formulation (F2) was58±1.800. The SD value was not significantly varies and it indicated that formulation

(F2) was meet the criteria for the weight variation as shown in table 2. Surface pH was varies in the range of 6.90±0.030 to 6.63±0.015 the formulation (F2) was shows pH range 6.81±0.050. Since this value was nearest to the saliva pH (i.e. 6.8) there was no irritation produce during the administration of films.

Folding endurance for all the formulation was found to be more than 100 folds. It shows that all formulation had a good plasticity. All the formulations were evaluated for the drug content. The result obtained was shown in table no. 2. The formulation (F2) shows maximum amount of drug i.e. 97.5±1.044 and less amount of drug was found in formulation F7. Disintegration time of each formulation was determined. It was varies in range between 22.1±1.33 sec to 40±1.10 sec. The disintegration time for the formulation F2 was found to be 22.1±1.33 sec. The In-vitro drug release study was carried out using USP dissolution test apparatus type-II. The result obtained was shown in table no.3. Formulation F2 shows 97.5% drug release, from table no.2 and table no.3 if we compared the disintegration time and dissolution, the decrease in disintegration time increase the rate of dissolution.

Table No. 2: Evaluation of Enalapril Maleate fast dissolving films.

Evaluation parameter						
Formulation code	**Thickness (mm)**	**Mean Weight (mg)**	**Drug Content %**	**Disintegration time (sec)**	**Surface pH**	**Folding Endurance**
F1	0.12±0.004	50±0.540	95.6±1.040	28.3 ± 1.527	6.82±0.036	>100
F2	0.18±0.004	58±1.800	97.5±1.044	22.1 ± 1.332	6.81±0.050	>100
F3	0.15±0.005	60±0.870	93.2±0.700	25.1 ± 1.742	6.80±0.045	>100
F4	0.22±0.003	52±0.900	91.7±0.871	30.2 ± 2.127	6.75±0.052	>100
F5	0.21±0.004	56±1.000	90.5±1.001	32.3 ± 2.345	6.90±0.030	>100
F6	0.25±0.005	60±0.930	94.5±0.360	32.7 ± 1.110	6.63±0.015	>100
F7	0.18±0.005	58±1.000	82.5±0.700	30.4 ± 0.980	6.84±0.025	>100
F8	0.12±0.107	55±0.660	84.5±0.300	34.6 ± 1.980	6.77±0.050	>100
F9	0.16±0.008	62±0.577	92.5±1.050	35.1 ± 1.227	6.84±0.036	>100

Table No. 3: Drug release study of Enalapril Maleate fast dissolving films.

% Drug release									
Time (min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
2	39.12±0.893	40.8±0.489	42.9±1.204	44.2±0.384	42.5±0.941	39.5±1.054	38.5±0.705	41.8±0.847	43.9±0.044
4	40.1±0.770	52.5±0.571	51.7±0.030	52.2±0.592	54.7±0.553	49.5±0.223	48.8±0.552	52.7±1.390	53.4±0.865
6	63.3±1.010	62.7±0.623	60.1±0.468	64.5±0.831	61.8±0.438	64.3±0.752	63.2±0.692	62.4±0.547	65.5±0.775
8	67.8±0.545	68.9±0.839	66.2±0.936	70.3±0.088	69.7±0.691	69.1±0.269	68.4±0.832	66.1±0.684	68.2±0.623
10	72.6±0.480	76.2±0.759	77.1±0.773	75.2±0.457	73.2±0.285	74.5±0.395	71.1±0.480	72.8±0.166	70.9±0.542
15	80.1±0.600	82.5±0.845	82.6±0.403	82.1±0.248	77.8±0.772	79.6±0.772	76.7±0.296	79.8±0.334	80.0±0.197
20	91.5±0.927	92.4±0.134	90.4±0.631	88.9±0.740	84.1±0.499	86.1±0.599	79.1±0.188	82.2±0.157	86.8±0.945
25	95.6±0.734	97.5±0.224	93.2±0.341	91.7±0.188	90.9±0.234	94.5±0.472	82.5±0.229	84.5±0.257	92.5±0.543

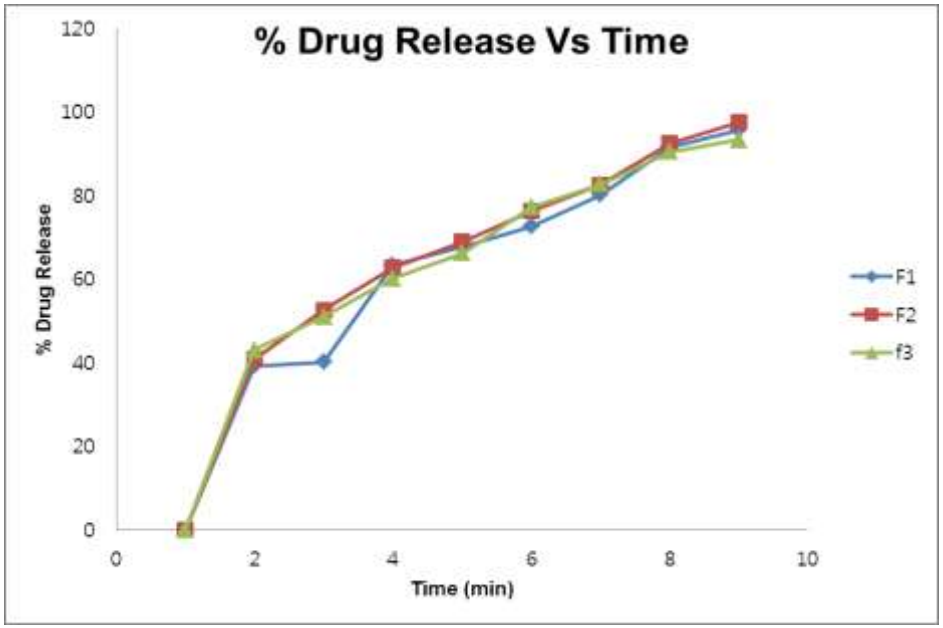

Fig.1: Drug release study of formulations F1, F2 and F3.

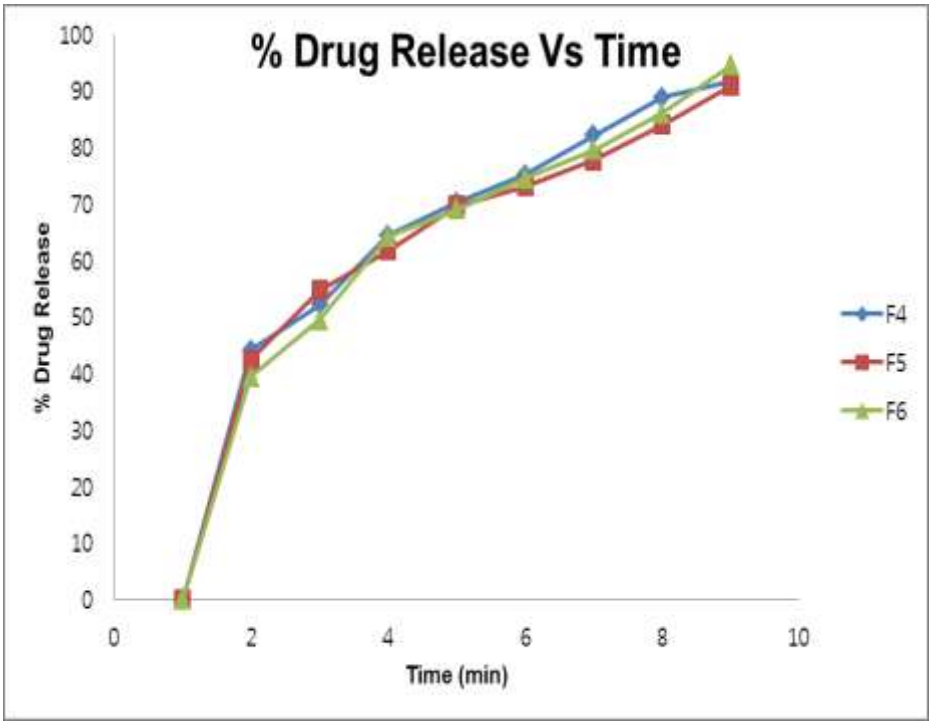

Fig.2: Drug release study of formulations F4, F5 and F6.

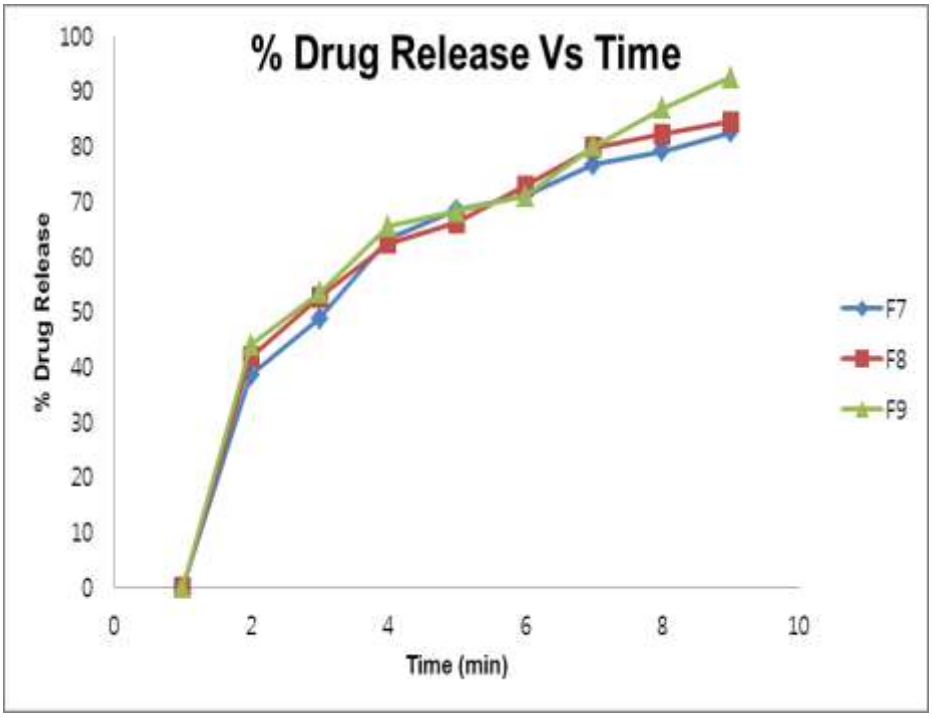

Fig. 3: Drug release study of formulations F7, F8 and F9.

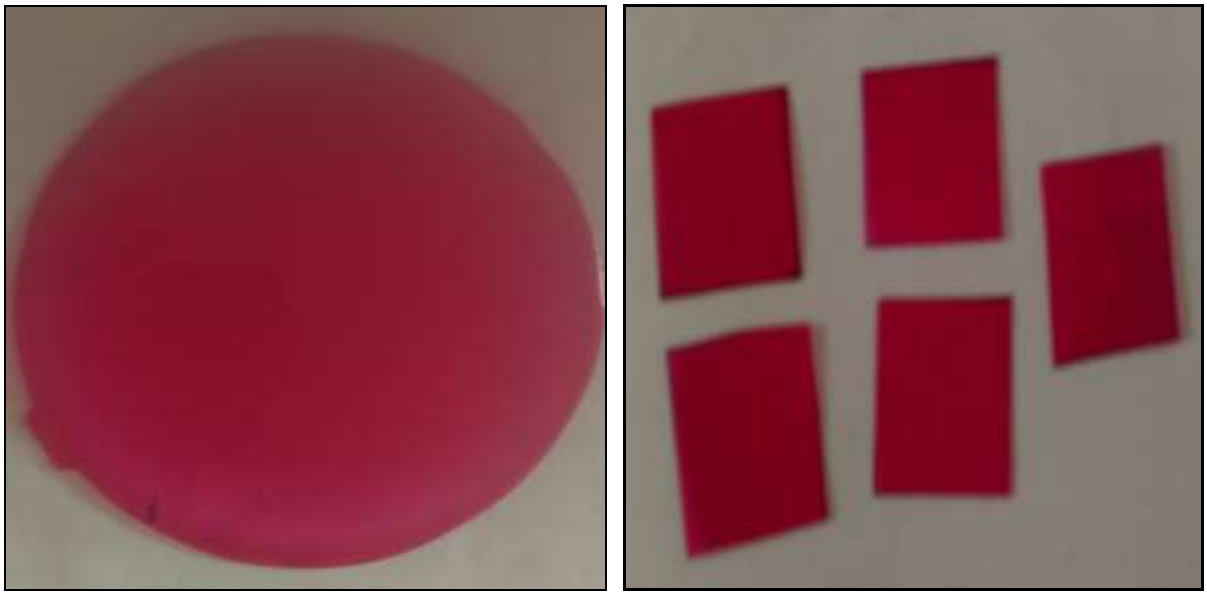

Fig. 4: Photographs of placebo and Enalapril Maleate Films.

ACKNOWLEDGEMENT

We are thankful to Mr. A.D. Maru Sir Principal of Loknete Dr. J.D. Pawar college of Pharmacy, Manur (Kalwan) for providing the facility to carry out the research work.

CONCLUSION

The results of the present study indicated that HPMC K15 and PVA could be used as a film forming polymer for formulation of fast dissolving film containing Enalapril Maleate. Acceptable mechanical properties were obtained for all the batches with invitro disintegration time of 22 s. On the basis of data obtained from in-vitro dissolution studies that F2 is promising formulation suitable for the immediate release of Enalapril Maleate for the systemic use since they exhibited maximum drug release and permeation respectively. The formulation batch F2 was found to be stable for a period of one month at 40°C/75%RH.

REFERENCES

1. Jui Trivedi, et al. Mouth Dissolving Film: A New Era in Pharma Field as a Conventional Dosage Form: A Review, International Journal of Pharmaceutical Research and Bio-Science, 2014; 3(1): 149-161.
2. Pallavi Patil, et al. Formulation, Evaluation and Optimization of Fast Dissolving Oral Film of Selective Antihypertensive Drug, World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(10): 996-1060.
3. Prabhakara Prabhu, et al. Formulation and Evaluation of Fast Dissolving Films of Lisinopril, Egypt Pharmaceutical Journal, 2015; 14: 56-54.

4. Ganesh R. Kulkarni, et al. Design and In-vitro Evaluation of Mouth Dissolving Film containing Amlodipine Besylate, World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(10): 925-945.
5. Vidhi Desai, et al. Formulation and Evaluation of Olmesartan Medoxomil Mouth Dissolving Film, Journal of Pharmaceutical Science and Bio-scientific Research (JPSBR), 2014; 4(3): 201-206.
6. Sravanthi R.R., et.al., "Mucoadhesive Buccal Films: An Innovative Drug Delivery System, International Journal of Pharm Tech Research, sep-oct 2014; 6(5): 1665-1678.
7. Thakur Smriti, Mouth Dissolving Films: A Review, International Journal of Pharma and Bio Sciences, 2013 Jan; 4(1): (P) 899-908.
8. Vaishali Y. Londhe, et.al. "Formulation, Development and Evaluation of Fast Dissolving Film of Telmisartan", Indian Journal Pharm Sciences, 2012; 74: 122-6.
9. Kulkarni Parthasarathi K. et al., Formulation and Evaluation of Mouth Dissolving Films Containing Rofecoxib, International Research Journal of Pharmacy, 2011; 2(3): 273-278.
10. A Semalty, et.al, "Formulation and Evaluation of Mucoadhesive Buccal Films of Enalapril Maleate," Indian Journal of Pharmaceutical Sciences, 2010; 72(s): 571-575.
11. Pravin Gavali, et.al, Design and "Development of Hydroxypropyl Methylcellulose (HPMC) based Polymeric Film of Enalapril Maleate", International Journal of Pharma Tech Research, Jan-Mar 2010; 2(1): 274-282.
12. Swati Swami, et al. Formulation and Evaluation of Fast Dissolving Oral Films of Metoprolol Succinate, International Journal of Engineering and Applied Sciences, 2015; 6(4): 28-38.
13. Sumedha Bansal, et al. Formulation and Evaluation of Fast Dissolving Films of An Antihypertensive Drug, International Journal of Pharmaceutical, Chemical and Biological Sciences, 2014; 3(4): 1097-1108.