World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 4.223

FORMULATING FAST DISINTEGRATING ZINC TABLET USING SINGLE STRUERS LABOPRESS-1

Okey-Mbata Chioma Chinyere[1,2]* Keatch Robert[3], Igwe Chidi[1] and Ukairo Doris[1]

[1]Department of Biochemistry, Federal University of Technology, Owerri.
[2]Department of Biomedical Engineering School of Engineering, Physics and Mathematics University of Dundee, Dundee, UK.
[3]Division of Mechanical and Electronic Engineering, University of Dundee, Dundee, UK.

***Corresponding Author: Okey-Mbata Chioma Chinyere**
Department of Biochemistry, Federal University of Technology, Owerri.

Article Received on 15/04/2017 **Article Revised on 04/05/2017** **Article Accepted on 25/05/2017**

ABSTRACT

The purpose of our research work was to formulate tablets of zinc as a nutritious element by direct compression method employing different disintegrants and ascorbic acid as an antioxidant at different proportions in addition to other excipients used in tablet formulation, in order to enhance the disintegration/dissolution rate as well as the percentage drug release. Pre-compression parameters which include bulk and tapped densities, Carr's index, Hausner's ratio were evaluated and found to be within acceptable limits. Weight variation, hardness, friability, disintegration time, and in vitro dissolution profile of the formulated tablets were evaluated. Following the data obtained from the dissolution study carried out in 900ml phosphate buffer of 0.05M, 6.8 pH at 37±1˚C, the best batch was found to formulations in batch I; because the formulations in this batch I were able to release 99.8% of the drug within 10 minutes. Furthermore, the data obtained were analyzed and found to be significantly difference at $p<0.05$.

KEYWORDS: Zinc, Superdisintegrant, Mould, Diarrhoea.

INTRODUCTION

Nowadays, and even in the past, many people are very scared of invasive method of taking drugs such as injections due to the fear of using sharp objects like needle, especially children of lower ages. In addition the dangerous risk of having the needle breaking into the body of a patient to cause another problem for the particular patient, the need for the development of very fast dissolving tablet with fast rate of the release of the active drug content is of great importance. Zinc deficiency could be as a contribution of many factors such as inadequate absorption of zinc in the body, typically noticed in vegetarians since they consume a lot of legumes and even whole grains which are known to have high content of phytates that can inhibit the absorption of zinc by binding to it. However, by soaking the grains and legumes in water for sometime before cooking can improve the bioavailability of zinc as recorded by the American Dietetic Association, Dietitians of CanadA.[1] Decreased absorption of zinc and increased excretion of zinc through the urine has been recorded in alcoholics due to excessive consumption of ethanol.[2] It has also been recorded that acute diarrhoea in humans especially children in the developing countries results to many number of mortality issues[3] hence supplementation has been recommended.[4,5] There are many superdisintegrants that have been employed in the development of fast dissolving oral tablets.[6,7] Antioxidants can cooperatively act in the presence of minerals,[8,9] have reported the advantage of using antioxidant in combination with minerals, as they have been found to act in synergistic and cooperative manner in addition to their individual action. Hence, it has been found necessary by our research team to develop a formulation that is capable of supplementing the essential micronutrient in the presence of ascorbic acid.

MATERIALS AND METHODS

Tablet formulation

The quantities of the compounds used in one tablet were calculated base the molecular weight of the metal, thus, 4.4g of zinc sulphate dehydrate was weighed out. The measured powdered compounds was mixed as outlined in table 1. The chemical compounds was measured using the weighing balance with ascorbic acid as the antioxidant and compressed into a round tablet of 10.00mm with the aid of a mold constructed to fit into the ram of Struers laboPress-1 machine at different forces and times.

Tablets' compression

This was carried out by employing a mold constructed to fit into the single punch compression machine (Struers LaboPress-1). The mold was made to have a hollow section in which the measured powdered mixture of the tablet formulation is poured into, so that it can be compressed into a 10.00mm diameter tablet with average of 5mm as the thickness.

Mold construction

The mold used in the tablet formulation was constructed to be a three-part single mold made of stainless steel alloy material, as shown in the figure below.

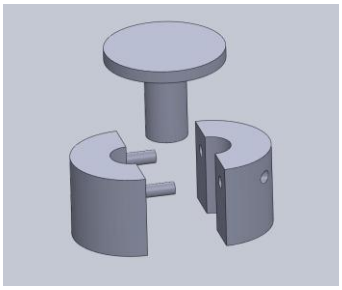


Figure 1: Diagram of a single mold made of three parts used in compression of the tablets formulated.

Evaluation of Preformulation parameters[10,11,12,13,14]

Repose angle

This was determined by the use of a rotating cylindrical chamber. The cylinder was gradually tilted, as soon as the powder mixture was noticed to have started slipping; the angle was measured using Solid handling study bench, Armfield, United Kingdom.

Hausner's ratio and Carr's index

These were calculated as outlined in the United States Pharmacopeia 2007 thus:

$$Hausner's\ Ratio = \rho tapped \div \rho bulk$$

$$Carr's\ Index = [(\rho tapped - \rho bulk) \div \rho tapped] \times 100$$

Bulk density and Tapped density

Loose bulk density ($\rho bulk$) of the powder mixture was calculated by dividing a known mass of the powder blend poured via gravity into a measuring cylinder by the bulk volume. Whereas the tapped density($\rho tapped$) was determined after tapping the powder mixture with hand until a constant value was obtained by considering the weight of the powder and the volume the powder mixture occupied in the cylinder after tapping.

Friability test

This test was carried out using the Roche friabilator. 18 tablets were weighed from each batch of the formulation and put in the friabilator chamber. The friabilator was rotated at 30 rpm for 5min after which the tablets were removed and weighed again and the friability was determined thus:

$$\%\ friability = [(Wb - Wa) \div Wa] \times 100$$

Where *Wb* is weight of tablet before the test.

Wa is weight of tablet after the test.

Hardness test

The tablets compressed at different forces of a given time were subjected to crushing test using the Monsanto hardness tester (Sheetal Scientific Industries, Mumbai, India) to determine the minimum load that can get them deformed or cracked.

Thickness

The thickness of 18 tablets from the various formulation batches was measured using a Vernier caliper, and the values represented as the mean ± standard deviation.

***In vitro* Dissolution test[14]**

Apparatus	: Dissolution apparatus I IP (Paddle)
Medium	: 6.8 pH phosphate buffer
Volume	: 900ml
Speed	: 50 rpm
Time	: 10 minutes
Temperature	: 37˚C ± 0.5˚C
λmax	: 214 nm

Statistical analysis

The statistical analysis was carried out using the SPSS version 16 software. The formulation experiments were performed in triplicate while the data were presented as mean ± standard deviation. Analysis of variance (ANOVA) was carried out using 95% level of confidence ($p<0.05$).

RESULTS AND DISCUSSION

Table 1: Composition of the formulated tablets.

Constituents	Batches											
	A	B	C	D	E	F	G	H	I	J	K	L
Zinc (mg)	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4
Methyl cellulose(%w/w)	50	50	50	50	50	50	50	50	50	50	50	50
Polyethylene glycol(%w/w)	1	1	1	1	1	1	1	1	1	1	1	1
Aerosil (%w/w)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Polyvinylpyrrolidone (%w/w)	2	2.5	5	0	0	0	0	0	0	2	2.5	5
Ascorbic acid (%w/w)	0	0	0	0	0	0	10	20	30	10	20	30
Croscarmellose (%w/w)	0	0	0	2	2.5	5	2	2.5	5	0	0	0
Mannitol (mg)	100	100	100	100	100	100	100	100	100	100	100	100

Precompression evaluation

The powder mixture of all the formulations were evaluated for angle of repose, tapped density, bulk density, Carr's compressibility index, and Hausner's ratio as shown in table 2 below, the values were represented as mean ± standard deviation of triplicate values of each formualation. All the values gotten for the precompression evaluation were within acceptable range which is an indication that the formulation mixtures have good flow property. The values obtained for the precompression evaluation are as follows: angle of repose (42.18˚±4.92˚ – 49.11˚±3.24˚); Carr's index (11.196%±0.998 – 12.611%±0.758); Hausner's ratio (1.128±0.048 – 1.144±0.054).

Table 2: Precompression evaluation of the formulation powder mixture.

Samples	Angle of Repose (˚)	Tapped Density (gm/L)	Bulk Density (gm/L)	Carr's Index (%)	Hausner's Ratio
A	48.22±4.11	0.669±0.054	0.593±0.059	11.36±0.711	1.128±0.048
B	42.18±4.92	0.681±0.023	0.597±0.044	12.335±0.59	1.141±0.039
C	45.32±5.18	0.663±0.069	0.587±0.036	11.463±0.980	1.129±0.051
D	48.22±5.21	0.671±0.035	0.592±0.023	11.773±2.400	1.133±0.071
E	47.32±3.01	0.635±0.034	0.558±0.037	12.126±0.961	1.138±0.064
F	43.57±4.18	0.681±0.057	0.591±0.031	12.041±2.973	1.137±0.044
G	46.28±3.92	0.674±0.061	0.589±0.029	12.611±0.758	1.144±0.054
H	45.19±5.51	0.681±0.057	0.597±0.054	12.355±3.241	1.141±0.061
I	49.11±3.24	0.634±0.048	0.562±0.061	11.356±1.495	1.128±0.059
J	43.24±4.33	0.652±0.039	0.579±0.052	11.196±0.998	1.126±0.066
K	46.81±4.71	0.66±0.026	0.577±0.028	12.576±2.156	1.144±0.032
L	47.23±4.23	0.658±0.055	0.581±0.031	11.702±1.979	1.133±0.049

Post compression evaluation

The various formulations were subjected to evaluation after compression by determining their average weight, thickness, hardness, friability and the values were respectively within the range as outlined: 111.154±0.28mg to 112.606±0.24mg; 4.86±0.05mm to 5.03±0.05mm; 3.09±0.33kg/f to 4.38±0.29kg/f to 4.38 ±0.29 kg/f; 0.51±0.12% to 0.83±0.51%. the details of this is as shown in table 3.

Table 4 is showing the values of the disintegration times of the formulations compressed with different forces at times. The optimized compression force was obtained by compression with the single punch compression machine (Struers LaboPress-1) using compression force of 10kN at 2minutes as the disintegration time was evaluated to be 0.67±0.13 for the formulations represented as "I".

Table 3: Post compression properties of formulated tablets.

Samples	Weight (mg)	Thickness (mm)	Hardness (kg/f)	Friability (%)
A	111.154±0.31	4.92±0.01	3.84±0.23	0.59±0.17
B	111.176±0.26	4.89±0.03	3.11±0.41	0.72±0.14
C	111.286±0.51	5.01±0.01	3.89±0.27	0.66±0.12
D	111.154±0.28	4.86±0.05	4.01±0.30	0.76±0.20
E	111.176±0.33	4.98±0.04	4.21±0.48	0.63±0.18
F	111.286±0.24	5.03±0.05	3.09±0.33	0.51±0.12
G	111.594±0.41	4.79±0.02	3.48±0.49	0.69±0.18
H	112.056±0.50	4.89±0.04	4.38±0.29	0.81±0.22
I	112.606±0.27	5.00±0.01	4.07±0.51	0.74±0.19
J	111.594±0.23	4.87±0.01	3.97±0.26	0.83±0.51
K	112.056±0.47	4.97±0.07	3.83±0.58	0.67±0.13
L	112.606±0.24	5.01±0.04	4.31±0.41	0.54±0.17

Table 4: Variation of disintergration time with respect to different compression forces and compression times.

Compression force (kN)	Formulation disintegration time (minutes)												Compression time (min)
	A	B	C	D	E	F	G	H	I	J	K	L	
45	8.89±0.11	8.70±0.13	8.61±0.14	8.26±0.11	8.05±0.13	7.90±0.10	7.48±0.12	7.29±0.12	7.09±0.13	7.89±0.12	7.74±0.13	7.66±0.11	30
45	7.40±0.21	7.36±0.12	7.31±0.13	7.22±0.11	7.15±0.16	7.09±0.21	6.82±0.15	6.71±0.13	6.69±0.12	6.97±0.11	6.92±0.11	6.86±0.14	20
45	6.71±0.18	6.66±0.10	6.48±0.10	6.42±0.15	6.39±0.11	6.34±0.14	6.07±0.13	6.01±0.11	5.98±0.11	6.27±0.10	6.20±0.14	6.19±0.12	15
45	5.99±0.20	5.96±0.12	5.91±0.13	5.78±0.12	5.58±0.14	5.49±0.11	4.87±0.11	4.70±0.14	4.56±0.11	5.04±0.11	5.01±0.23	4.90±0.11	5
10	0.98±0.14	0.89±0.15	0.85±0.11	0.79±0.11	0.78±0.15	0.75±0.13	0.71±0.12	0.70±0.12	0.67±0.13	0.74±0.13	0.74±0.11	0.72±0.10	2
15	2.18±0.13	2.01±0.13	1.98±0.14	1.88±0.13	1.68±0.12	1.62±0.12	1.28±0.11	1.25±0.11	1.22±0.16	1.48±0.21	1.42±0.23	1.34±0.13	2
20	3.42±0.14	3.20±0.16	3.01±0.12	2.98±0.13	2.28±0.14	2.26±0.21	1.99±0.14	1.91±0.11	1.89±0.14	2.11±0.11	2.09±0.12	2.02±0.12	2
25	3.67±0.16	3.62±0.12	3.60±0.11	3.53±0.14	3.51±0.13	3.44±0.14	3.04±0.12	3.01±0.13	2.98±0.11	3.43±0.11	3.12±0.11	3.06±0.10	2

The cumulative drug release (%) was determined for each of the formulations by subjecting them to in vitro dissolution studies. After 10 minutes, the formulation batch represented as I was found to release up to 99.8% of the drug. While the batch labeled A showed the least drug release % amongst the other formulations with the value of its drug release as 84.98%. Table (5) below shows the summary of cumulative drug release of the various formulation batches statistically analysed at $p<0.05$.

Table 5: summary of the cumulative drug release of the various formulation batches.

Groups		Time (minutes)				
	0	2	4	6	8	10
1	0	87.56±3.07^{ab}	88.13±3.34^{ab}	88.54±3.41^{ab}	88.99±3.33^{ab}	90.28±3.98^{ab}
2	0	88.99±4.33^{ab}	89.41±3.88^{ab}	89.92±4.11^{ab}	90.32±3.83^{ab}	91.33±4.54^{ab}
3	0	90.42±3.87^{ab}	91.28±3.38^{ab}	91.73±3.87^{ab}	92.93±4.62^{ab}	93.26±4.50^{ab}
4	0	84.05±1.75^{a}	85.30±2.74^{a}	85.73±2.61^{a}	86.30±2.42^{a}	86.73±2.41^{a}
5	0	90.01±0.84^{ab}	90.39±0.80^{ab}	90.37±0.76^{ab}	91.45±0.84^{ab}	91.78±0.89^{ab}
6	0	92.98±2.71^{b}	93.56±2.64^{b}	94.67±2.82^{b}	95.58±3.78^{b}	97.02±2.67^{b}
7	0	89.43±0.84^{ab}	89.79±0.33^{ab}	90.04±0.39^{ab}	90.48±1.04^{ab}	91.83±0.17^{ab}
marketed drug	0	45.09±1.43^{c}	48.11±1.32^{c}	49.84±2.05^{c}	50.64±1.41^{c}	50.72±1.65^{c}
pure drug	0	20.74±0.75^{d}	21.78±0.62^{d}	22.02±1.41^{d}	24.98±0.78^{d}	30.71±0.96^{d}

Values are mean ± standard deviation. Values with different superscript letter(s) per column are statistically significant ($p<0.05$).

Foot note

Groups Constituent

1- 2% Croscarmellose as superdisintegrant
2- 2.5% Croscarmellose as superdisintegrant
3- 5.0% Croscarmellose as superdisintegrant
4- Polyvinylpyrrolidone as ordinary/normal disintegrant
5- 2% superdisintgrant and 10% ascorbic acid
6- polyvinylpyrrolidone and ascorbic acid
7- 5% superdisintgrant and 30% ascorbic acidhe

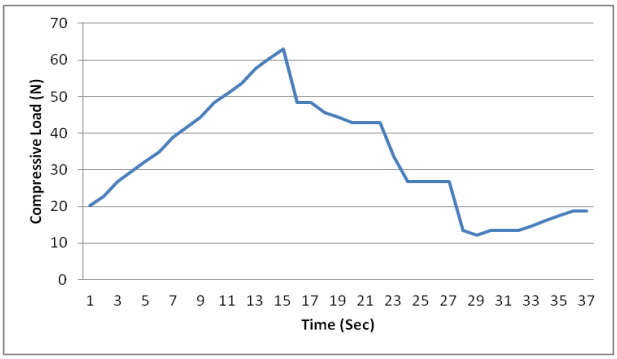
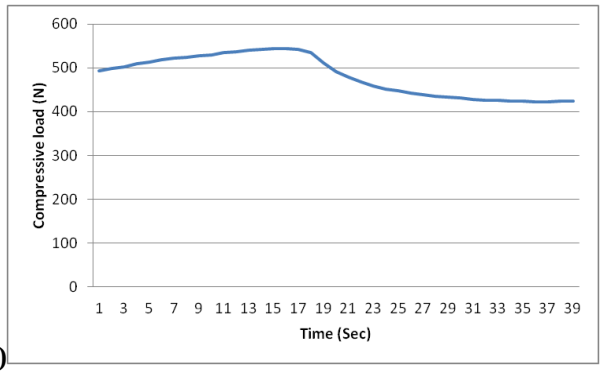
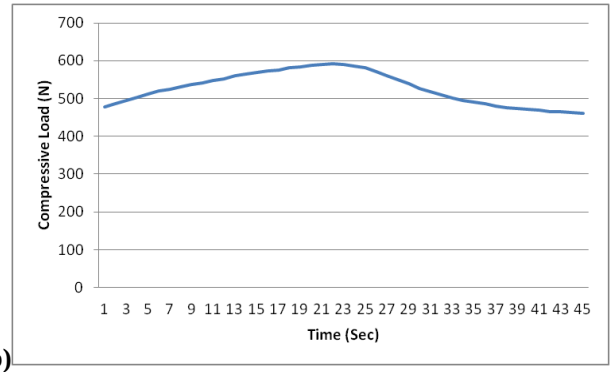


Figure 2: crushing test results of tablets formulated at 15kN for 2minutes.



(a)

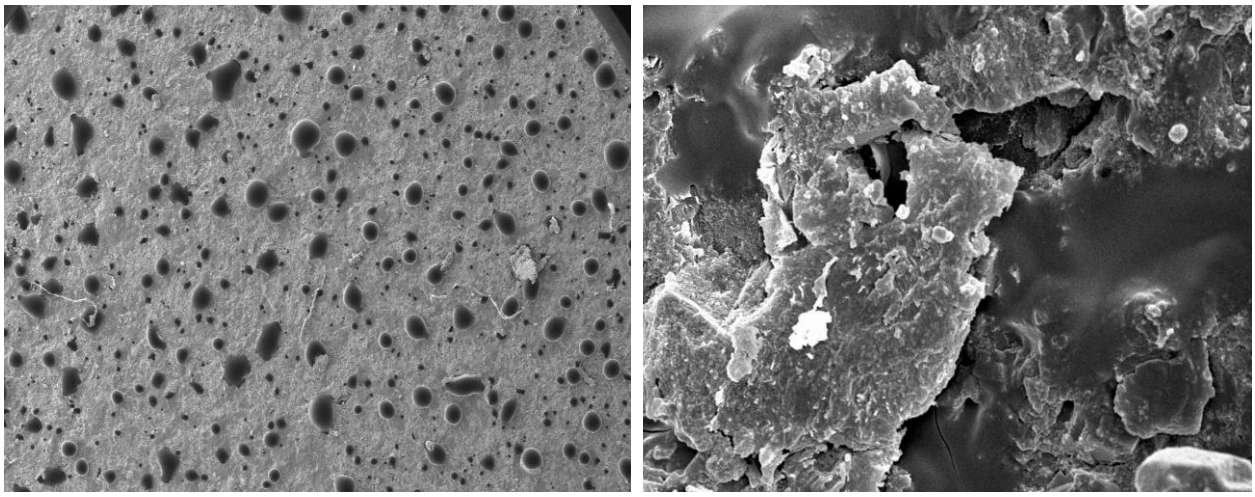


(b)

Figure 3: graphical representation of crushing test for formulation at 45kN for 5minutes (a) and 10minutes (b) respectively.

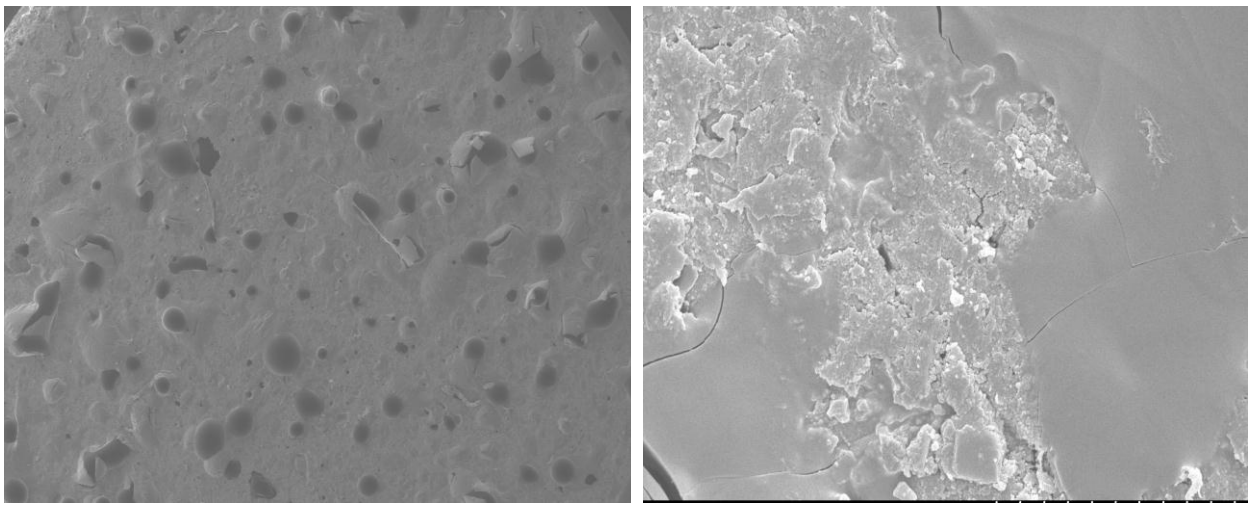
Crushing test

The formulations were subjected to crushing test to ascertain how easily the various tablet formulations can be broken under an external force. Figures 2 and 3 above shows that the formulations with less compression force cracked under a much reduced compressive load and less time (figure 2), where as the formulations with higher compressive force were somehow reluctant to crack even under a very high compressive load. These compressed tablet were also examined under the scanning electron microscope and the structural photographs obtained as shown in the figures 4 and 5 indicated that at lower time and reduced force applied, the formulations were more porous than those compressed using higher force at longer time, hence their differences in the disintegration time and crushing test.



(a) **(b)**

Figure 4: Scanning electron microscopic photograph of tablet formulated at 45kN for 5minutes, taken at X30 (a) and X2500 (b) magnifications.



(a) **(b)**

Figure 5: Scanning electron microscopic photograph of tablet formulated at 45kN for 10minutes, taken at X30 (a) and X2500 (b) magnifications.

CONCLUSION

The formulated zinc tablet is a very good development that can certainly contribute positively to the control of diarrhoea and zinc deficiency in many countries especially in the less developed communities where there are inadequacy micronutrients in the nutritional composition of the populace. This formulation with a single punch compression machine (Struers LaboPress-1) at optimized force and time is a great achievement as the disingration time of the formulated tablets were much reduced as well as the there was increased cumulative drug release in the presence of superdisintegrant, hence this our research work has been found relevant to be continued in the direction of further analysis on the formulated tablets.

ACKNOWLEDGMENT

The authors will like to thank the Tertiary Education Trust (TET) fund for their support in carrying out the study.

REFERENCES

1. American Dietetic Association, Dietitians of Canada. Position of the American Dietetic Association and Dietitians of Canada: Vegetarian diets. J Am Diet Assoc, 2003; 103: 748-65.
2. Navarro S, Valderrama R, To-figueras J, Gimenez A, Lopez JM, Campo E. Role of Zinc in the process of pancreatic fibrosis in chronic alcoholic. Pancreas, 1994; 9: 270-4.
3. Chasapis C, Loutsidou A, Spiliopoulou C, Stefanidou M. Zinc and human health: an update. Arch. Toxicol, 2012; 86(4): 521-534.
4. World Health Organization and United Nations Children Fund. Clinical management of acute diarrhea. WH/UNICEF Joint Statement, August 2004. [http://www.unicef.org/nutrition/files/ENAcuteDiarrhoea reprint.pdf].
5. Liberato SC, Singh G, Mulholland K, Zinc supplementation in young children: a review of the literature focusing on diarrhoea prevention and treatment. Clin. Nutr, 2015; 34 (2): 181-188.
6. Mathews MM, Kilimozhi D, Kuppuswamy S. Formulation, Characterisation and Comparative Invitro - Invivo Evaluation of Orodispersible Tablets of Satranidazole Solid Dispersion. Indo American Journal of Pharmaceutical Research, 2016; 6(04): 5024-5032.
7. Carocho M, Ferreira ICFR. A review on antioxidants, prooxidants and related controversy: Natural and synthetic compounds, screening and analysis methodologies and future perspectives. Food Chem. Toxicol, 2013; 51: 15–25.
8. Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malyy D, Roussel A, Favier A, Briançon S. The su.vi.max study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. Arch. Int. Med, 2004; 164(21): 2335–2342.
9. Natarajan R, Vaishnani R, Rajendran NN. Formulation and Evaluation of Immediate Release Tablets of Paroxetine HCl Using Different Superdisintegrants, IJRPBS, 2011; 2(3): 1095-1099.
10. Syed A. Immediate Release Drug Delivery Systems: A Review. IJBTR, 2001; 1: 24-29.
11. Vinod J, Chenthilnathan A.Formulation & In-vitro evaluation of immediate release tablets of losartan potassium using different superdisintegrants. JBPR, 2013; 2: 25-30.
12. Roshan P, Uttam B, Panna T. Formulation of once a day controlled release tablet of indomethacin based on HPMC –Mannitol. KUJSET, 2008; 1: 55-67.
13. Mohire NC, Yadav AV, Gaikwad VK. Novel approaches in development of Metronidazole orodispersible tablets. Research Journal of Pharmacy and Technology, 2009; 2: 283-286.
14. The United States Pharmacopeial Convention, Inc. *USP 30*, 2007. General chapter *Disintegration,* 701: 276.