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FORMULATION AND EVALUATION OF *CARICA PAPAYA* LEAVES AQUEOUS EXTRACT CHEWABLE TABLETS

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ABSTRACT

The objective of the present study is to formulate and evaluate *Carica papaya* leaves aqueous extract chewable tablets. *Carica papaya* leaves aqueous extract exhibited potential activity against Dengue fever. *Carica papaya* leaves are a rich source of complex biochemical constitutes including flavonoids, glycosides, alkaloids, glutathione and glucosinolates that helps boost the number of platelets by stimulating bone marrow and it responsible for production of platelets. The direct compression method was used for the preparation of chewable tablets. *Carica papaya* chewable tablets were characterized by weight variation, hardness, friability, drug content uniformity, dissolution and short-term stability studies. These tablets are intended to disintegrate smoothly in the mouth at a moderate rate either with or without actual chewing, characteristically chewable tablets have a smooth texture upon disintegration, are pleasant taste. Geriatric and pediatric patients and travelling patients who may not have ready access to water are most need of easy swallowing dosage forms like chewable tablets. In this study the formulation *In-vitro* drug release studies revealed that the cumulative % drug release of *Carica papaya* chewable tablets was found to be 86.3%. The bulk density and tapped density of the formulation was found to be 0.588gm/ml and 0.800gm/ml respectively. The result of Carr's compressibility index and Hausner's ratio for the formulation shows fair flow properties.

KEYWORDS

Carica papaya leaves aqueous extract, Dengue fever, Platelet count, Chewable tablets and Direct compression method.

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INTRODUCTON

Dengue, a viral disease transmitted by the bite of the Aedesmosquito. Dengue Hemorrhagic Fever (DHF) is a mosquito-borne infection which in recent decades has become a major international public health problem. Dengue is prevalent in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban areas. It has

become a major public health problem. Today dengue fever affects most Asian countries and has become a leading cause of hospitalization and death among children in the region. One of the most problem of dengue is that there are no effective antiviral agents available to treat dengue complications ,Up to date there is no specific treatment for dengue fever Ayurvedic literature reveals that papaya (*Carica Papaya*) leaf extract has haemostatic and other medicinal properties that could be utilized very much in treatment of dengue. A herbal medicine being investigated to control the mammoth problem of dengue is the extract of the leaves of the papaya plant, *Carica papaya*. There have been conflicting reports on the effectiveness of this extract in the treatment of dengue. In this article, we present the use of the papaya leaf extract for the treatment of dengue. Since from earlier days the papaya has been used for the treatment of several diseases.

The papaya leaves, fruits and seeds has various beneficial effects and suggested for scientific studies. The papaya leaves extract plays a major role to treat digestive disorders. The extracts from fruits and seeds have bactericidal properties. Papaya fruit juice and leaf aqueous extract are also produce beneficial effects in various diseases like anticancer, antioxidative, anti-inflammatory, anti-bacterial, nephroprotective, hepatoprotective, hypoglycemic and hypolipidemic effects, and anti-sickling effect in sickle cell disease. *C. papaya* L. leaf extracts inhibits heat-induced and hypotonicity-induced hemolysis of erythrocytes present in both healthy individuals and individuals with dengue infection. The extracts are likely to possess membrane-stabilizing properties and protect blood cells against stress-induced destruction. Papaya leaves contains flavonoids and other phenolic compounds, these constituents mainly useful in preventing platelet lysis, this property might be helpful in patients with dengue infection.

MATERIAL AND METHODS

Materials

Carica papaya aqueous extract was extracted in laboratory, Tri basic calcium phosphate, sucrose, talc, magnesium Stearate and vanilla powder purchased from UV Scientifics, Hyderabad-500074.

Extraction process

Fresh leaves of *Carica papaya* were collected during July. Fresh leaves were collected, washed with water and wiped with a clean cloth to remove dust. Leaves were shade dried at room temperature and powdered using a mixer grinder. 30 g of powdered plant material was extracted with 300 ml water in an Ultrasonicator at 37ºC for 2 h. The extract thus obtained was concentrated and evaporated to dryness on a water bath maintaining the temperature at 70ºC.

Determination of λ_{max}

Concentration of 120µg/mL of *Carica papaya* aqueous extract dissolved in phosphate buffer pH 7.4 separately scanned over a wavelength range of 200-800nm and the wave length found to be 238nm.

Standard calibration curve of *Carica papaya* aqueous extract by UV

The UV absorbance of *Carica papaya* aqueous extract standard solution in the range of 2 to 10µg/mL in phosphate buffer pH 7.4 showed linearity at λmax 238 nm. The linearity was plotted for absorbance against concentration with R2 value 0.999 for phosphate buffer

Preparation of Standard Calibration Curve of *Carica papaya* Aqueous Extract

10 mg of *Carica papaya* aqueous extract was dissolved in 10 ml of phosphate buffer pH 7.4 separately to give a stock solution of 1000µg/mL. From the stock solution, the standard solutions with concentrations ranging from 2-10µg/mL were obtained. The absorbance of these solutions was observed at 238 nm. These absorbance values were used to prepare the standard plot

PREPARATION OF CHEWABLE TABLETS

Method

All powder compounds were accurately weighted, passed through a standard sieve (sieve no 80) and thoroughly blended for 5 min. After being mixed powders were evaluated for bulk density and tapped density, compressibility index (Carr's index), Hausner's ratio and angle of repose. Chewable

tablets were prepared by direct compression using rotary tablet compression machine.

Pre-Compression Studies

Physical appearance

The physical appearance of the tablet was studied visually in shape, colour, texture and odour.

Angle of repose

It is the maximum angle that can be obtained between the freestanding surface of powder heap and the horizontal plane. It was determined by using fixed funnel method. Specified amount of powder drug was transferred to the funnel keeping the orifice of the funnel blocked by the thumb. When the powder was cleared from funnel then measured its angle of repose and measured in θ.

Angle of repose $\theta = \tan^{-1} (h/r)$

Bulk density

Bulk density is defined as the mass of a powder divided by the bulk volume.

Bulk density (b) = M/V_b (Where, M is the mass of the sample, Vb- bulk volume)

Tapped density

Tapped density is defined as ratio of total mass of the powder to the tapped volume of powder

Tapped density (t) = weight of powder blend/Minimum volume occupied by cylinder

Compressibility indices

Carr's index

It was determined by using tapped density and bulk density of the powder mixture.

$$\text{Carr's index} = \frac{\text{Tapped density-Bulk density}}{\text{Tapped Density}} \times 100$$

Hausner's ratio

It is an indirect index of ease of measuring of powder flow Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25)

Hausner's ratio = Tapped density/Bulk density

Post-Compression Studies Of Prepared Tablets

The tablets were evaluated for various parameters after consideration of pre-formulation to overcome errors during formulation preparation.

Thickness

The tablet thickness was calculated by Vernier callipers. Tablet was put in between two jaws vertically and measured thickness and expressed in mm.

Weight variation

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance. The individual weighed is then compared with average weight for the weight variations. The weight variation test would be a satisfactory method of determining the drug content uniformity of tablets.

$$\%\text{deviation} = \frac{\text{Individual weight-average weight}}{\text{Average weight}} \times 100$$

Hardness

Hardness is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The hardness was tested using Monsanto tester. For determination of hardness factor, the average of the six determinations was determined and reported. The force was measured in kilograms per centimeter square.

Friability

To evaluate the degree of friability of the tablets from each batch, ten tablets were randomly selected, dusted and weighed. The tablets were placed in a Roche friabilator and subjected to its tumbling action at 25 revolutions per minute for 4 minutes. Then after, the tablet were once again dusted and reweighed to determine the % loss of weight.

$$\text{Friability} = \frac{\text{Weight of the tablet before test- weight of the tablet after test}}{\text{Weight of the tablet before test}} \times 100$$

***In vitro* drug release**

In vitro drug release studies were undertaken using USP apparatus 2 (paddle method). The dissolution medium was 900 ml phosphate buffer of pH 7.4 at 37 ± 0.5°C at a stirring rate of 75 rpm. During rotations, 5ml of sample was withdrawn at 5 min interval and replaced with fresh medium to maintain sink condition. Samples were filtered using Whatsman filter paper and taken absorbance in UV at 238 nm.

Stability studies

The formulated tablets were subjected to stability studies at 4ºC ± 2ºC and 25ºC ± 2ºC. The products

were evaluated for physical characteristics over a period of 3 months.

RESULTS AND DISCUSSION

The chewable tablet was formulated by direct compression method. This technique was used for a tablet which minimizes processing steps and eliminated wetting and drying process. The physiochemical property shows satisfactory results by a tablet which are within the range of prescribed standards required for investigation of the present study. Tablets were examined on the basis of weight uniformity (Denver Instrument), friability (Roche friabilator), hardness (Monsanto hardness tester), and estimation of drug content (UV-Visible spectrophotometer) using calibration curve. The dissolution test was made in accordance with USP type II (LAB INDIA), 75rpm speed, at a temperature of 37°C, pH 7.4 phosphate buffer. Amount of drug release was measured in the intervals of 10, 20, 30, 40, 50, and 60 min and determined by UV-Visible Spectrophotometer (Model No: 2450) using calibration curve. All tests were made in accordance with the Indian Pharmacopeia and the United States Pharmacopeia.

Preformulation

Flow properties

The values obtained are reported in the Table No.3. The powder flow properties of *Carica papaya* aqueous extract were studied to evaluate compressibility of the drug, since it has to be formulated as tablet. The results obtained are bulk density 0.588 mg/ml and tapped density was 0.800 mg/ml and Hausner's ratio 1.36. The results showed that the compressibility of the formulation was 26.5% .which indicate that the drug has poor flow properties.

Particle Size Analysis

According to USP32 By the above results it was observed that the 81.5% of particles are retained on the #140 mesh which have 106µm aperture size and 83.60% of particles are passed through the #100 mesh which have 150µm aperture size. Therefore it was concluded that major amount of particles have its size range of 150 µm to 106 µm.

Discussion

In the present study an attempt has been to formulate and evaluate *Carica papaya* chewable tablets by direct compression method, pharmaceutically acceptable easily available inert excipients were used for the preparation of *Carica papaya* chewable tablets. The prepared formulation was subjected to both pre and post formulation studies. The drug sample showed similar results as reported.

Solubility

Solubility of drug is important factor affecting its release from drug delivery system. Hence solubility analysis of *Carica papaya* chewable tablets was done. The solubility of the formulation was determined and found to be freely soluble in water.

UV spectroscopic analytical method

Standard curve of *Carica papaya* chewable tablets as shown in Table No.2 wavelength of maximum absorption was found to be 238nm. The *Carica papaya* chewable tablets obeyed the Beer's-Lambert law in concentration range of 2-10µg/ml at this wavelength. This is well correlated with the reported value (238nm).

The tablets are prepared by direct compression method

The powder blend were evaluated for various flow properties. The powder blend showed poor flow properties evident from the results shown in Table No.3. The angle of repose values were ranged from 32.06.the results were found to be above 30; hence they have poor flow ability. The carr's index ranged from 13.8 and hausner's ratio value ranged from 1.43 hence they have poor flow and poor flow ability.

PHYSICAL CHARACTERIZATION OF CARICA PAPAYA CHEWABLE TABLETS

Tablet thicknesses, hardness, weight variation, friability of formulated tablets are presented.

Uniformity of weight

All the prepared tablets of *Carica papaya* chewable tablets were evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ±7.5%.

Hardness and friability

The hardness of the tablet formulation was found to be in the range of 4 to 5 kg/cm^2. The friability values were found to be in the range of 0.5-1%.

***In-vitro* dissolution study**

In-vitro dissolution studies were performed in pH 7.4 buffer. In the dissolution studies the formulated tablet showing better drug release up to 6 hrs.

Stability Studies

Carica papaya aqueous extract chewable tablets were stored at room temperature and refrigerated temperature for 3 months. At the temperature of 4ºC ± 2ºC, there was no significant change in physical and chemical properties of formulated tablets. There was a change in physical properties of tablets at 25ºC ± 2ºC after 1 month. Thus, it can be stated that tablets showed good storage stability at 4ºC ± 2ºC.

Table No.1: Composition of chewable tablets

S.No	Ingredients	Amounts (mg)
1	Carica papaya aqueous extract(API)	250
2	Di basic calcium calcium phosphate(Dry binder and filler)	149
3	Sucrose(sweetening agent)	90
4	Magnesium Stearate(lubricant)	5
5	Talc (glidant)	5
6	Vanilla powder(flavouring agent)	1

Table No.2: Standard calibration curve for *Carica papaya* aqueous extract

S.No	Concentration in µg/ml	Absorbance at 238nm
1	0	0
2	2	0.16
3	4	0.34
4	6	0.51
5	8	0.67
6	10	0.86

Table No.3: Flow properties of powder blend

S.No	Wt (g)	V_0 (ml)	V (ml)	Bulk density (g/ml)	Tapped density (g/ml)	Compressibility index	Hausner's Ratio
1	20	34	25	0.588	0.800	26.5%	1.36

Table No.4: Particle size analysis of *Carica papaya* aqueous extract

S.No	Mesh No	Pore size*	W_o	W1	W1- W_o	% Retained
1	#60	250 µm	345	345	0	0%
2	#80	180 µm	348.7	350.85	2.15	4.30%
3	#100	150 µm	335.8	344.9	4.55	9.10%
4	#140	106 µm	368.8	409.55	40.75	81.50%
5	#200	75 µm	329.5	331.35	1.85	3.70%
6	Blank	-	518.3	519	0.7	1.40%

Evaluations of *Carica Papaya* Aqueous Extract Chewable Tablets by Direct Compression Method

Physical evaluation of tablets

Table No.5: Physical Evaluation of tablets

S.No	Parameters	F
1	Weight(mg)	500
2	Colour	Pale green
3	Surface	Smooth
4	Thickness(mm)	4.8
5	Hardness(Kp)	4 kg/cm2
6	% weight variation	2.5
7	Friability (%)	0.5%

Pre compression parameters

Table No.6: Pre compression parameters

S.No	Parameters	F
1	Bulk Density	0.5
2	Tapped Density	0.71
3	Angle of repose	32.06
4	Carr's index	13.8
5	Hauser's Ratio	1.43

Dissolution profiles of chewable tablets

Table No.7: % Cumulative Drug Release of tablets

S.No	Time in min	%CDR
1	0	0
2	10	19.4
3	20	34.2
4	30	49.6
5	40	62.5
6	50	74.4
7	60	86.3

Figure No.1: Image of papaya leaves

Figure No.2: Image of *Carica papaya* dried leaves powder

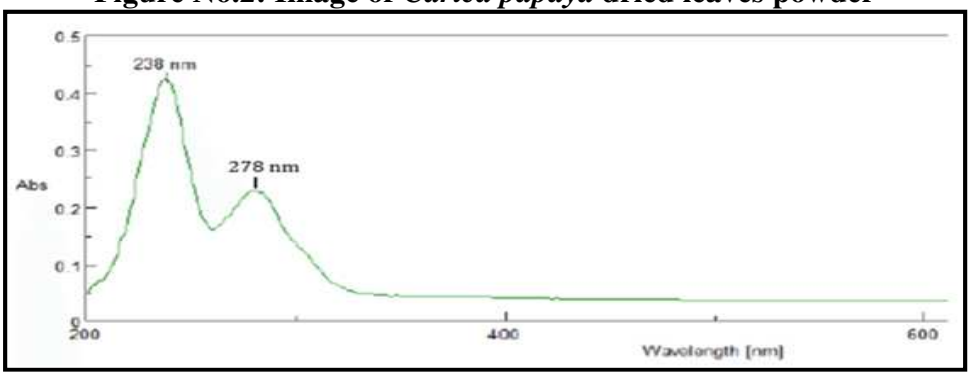

Figure No.3: UV- Visible spectra of C. papaya Aqueous Extract

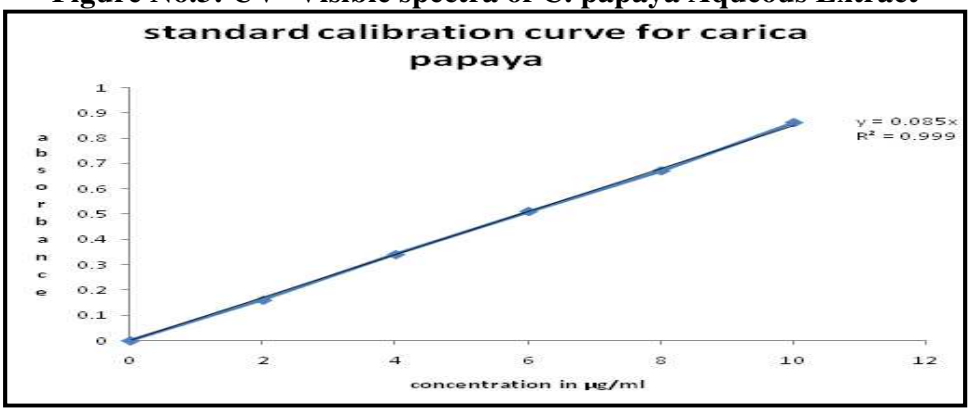

Figure No.4: Calibration curve for *Carica papaya* aqueous extract

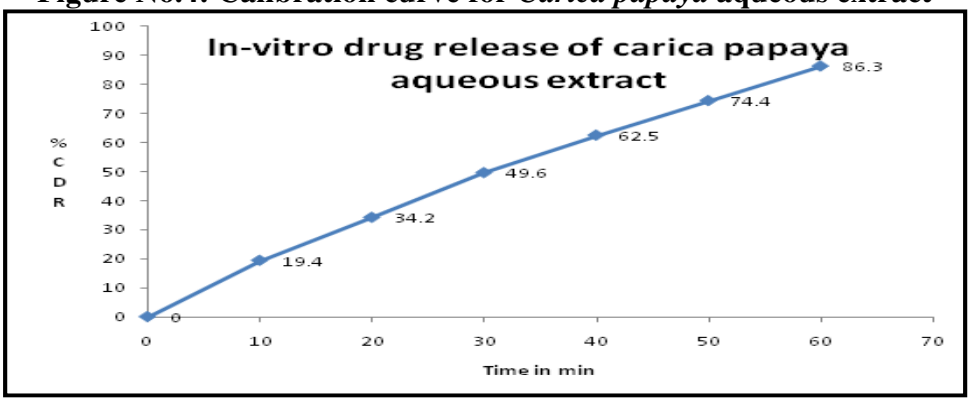

Figure No.5: *In-vitro* drug release of *Carica papaya* aqueous extract

CONCLUSION

In the present research work, an attempt was made to formulate chewable tablets of *Carica papaya* aqueous extract by direct compression method. *Carica papaya aqueous* extract was formulated as chewable tablets. Drug- excipient compatibility was confirmed by FT-IR studies. Pre compression studies showed fair flow ability and complied the pharmacopeial requirement for tablet properties. From the in vitro drug release profile studies, tablet shows immediate drug release due to the direct compression and release was found to be uniform and showed more than 80% drug release over a period of 60 min. Hence, formulation and development of *Carica papaya* aqueous extract as chewable tablet can be further exploited and investigated for its activity against symptoms of dengue fever.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. Aruoma O I, Deiana M, Rosa A, Casu V, Piga R, Peccagnini S, Dessi M A, Ke B, Liang Y F and Higa T. Assessment of the ability of the antioxidant cocktail-derived from fermentation of plants with effective microorganisms (EM-X) to modulate oxidative damage in the kidney and liver of rats *in vivo*, studies upon the profile of poly-and mono-unsaturated fatty acids, *Toxicol Lett,* 135(3), 2002, 209-217.
2. Chavkin *et al.* chewable molded tablets containing medicinally active substances, United state patents, 5, 753, 255, 1998.
3. Giordanir, Slepalo M, Moulin-Traffort J and Reglip. Antifungal action of *Carica papaya* latex, isolation of fungal cell wall hydrolyzing enzymes, *mycoses,* 34(11-12), 1991, 469-477.
4. Javed H, Shah S. Formulation and Evaluation of Taste Masked Doxycycline HCl Medicated Jelly, *Der Pharmacia Sinica,* 8(2), 2017, 33-39.
5. Cebra J J. The Use of Water-Insoluble Papain for Structural Studies of the Products of Antigen-Antibody Interaction Plastic and Reconstructive Surgery, 30(1), 1962, 213-214.
6. Kakali Bandyopadhyay and Santinath Ghosh. Preparation and Characterization of Papain-Modified Sesame (Sesamumindicum L.) Protein Isolates, Department of Chemical Technology, University of Calcutta, 92 Acharyya Prafulla Chandra Road, Kolkata 700 009, West Bengal, *India Journal of Agricultural and Food Chemistry,* 50(23), 2002, 6854-6857.
7. Kathiresan K, Vijin P, Moorthi C, Manavalan R. Formulation and Evaluation of loratadine chewable tablets, *Research Journal of pharmaceutical, Biological and Chemical Sciences,* 1(4), 2010, 763-774.
8. Khar R K, Sohi H. Taste masking technologies in oral pharmaceuticals: Recent development and approaches, *Drug. Dev. Ind. Pharma,* 30(5), 2004, 429-448.
9. Lachman L, Liberman H A, Kanig L J. Theory and Practice of Industrial Pharmacy, *Vargese Publication House,* 3rd Edition, 1990, 293-336.
10. Lachmann L, Liberman H A, Schwartz J B. Pharmaceutical Dosage Forms, *New York: Marcel Dekker Inc,* 2(1), 1989, 616.
11. Mangala B Murthy, Bhasker K Murthy, Sanjay Bhave. Comparison of safety and efficacy of papaya dressing with hydroge peroxide solution on wound bed preparation in patients with wound gape, *Indian Journal of Pharmacology,* 44(6), 2012, 784-787.
12. Mishra B, Sharma G. Investigation of organoleptic characteristics in the development of soft chews of calcium carbonate as mineral supplement, *Yakugaku Zasshi,* 129(12), 2009, 1537-1544.
13. Mojica-Henshaw M P, Francisco A D, De Guzman F and Tingo X T. Possible Immunomudulatory actions of *Carica papaya*

seed extract, *Clin Hemorheol Microcirc,* 29(3-4), 2003, 219-229.
14. Nanda A R, Garg K S. An update on taste masking technologies or Oral pharmaceuticals, *Indian Journal Pharma. Sci,* 64(1), 2002, 10-17.
15. Oderinde O, Noronha C, Oremosu A, Kusemiju T and Okanlawon O A. Abortifacient properties of aqueous extract of *Carica papaya* Linn. Seeds on female Sprague-Dawleyrats, *Niger Postgrad Med J,* 9(2), 2002, 95-98.
16. Patel H, Shah V, Upadhyay U. New pharmaceutical excipients in solid dosage forms, *International Journal of pharmacy and Life Sciences,* 2(8), 2011, 1006-1019.
17. Patel Y, Shukla A, Saini V, Shrimal N, Sharma P. Chewing Gum as a drug delivery system, *International Journal of Pharmaceutical Sciences and Research,* 2(4), 2011, 748-757.
18. Patil J, Vishwajith V, Gopal V. Formulation Development and Evaluation of Chewable Tablets Containing Non Sedating Antihistamine, *Journal of Pharmaceutical and Scientific Innovation,* 1(3), 2012, 112-117.
19. Pundir S, Verma A M. Oral disintegrating preparation -medicated chewing gum, *Pharma Utility,* 8, 2014.
20. Rahmat A, Abu Bakar M F, Faezah N and Hambali Z. The effects of consumption of guava (Psidiumguajava) or papaya (*Carica papaya*) on total antioxidant and lipid profile male youth, *Asia Pac J Clin Nutr,* 13(Suppl), 2004, S106.
21. Raja Manali M, Dhiren P. Oral medicated jelly: a recent advancement in formulation, *An international Journal of Pharmaceutical Sciences,* 7(2), 2016, 13-20.
22. Ray C, Arora V, Sharma V. Fast dissolving tablets-A Novel drug delivery system for pediatric and geriatric patient, *International Bulletin of drug Research,* 1(2), 2012, 55-70.
23. Rimbach G, Park Y C, Guo Q, Moini H, Qureshi N, Saliou C, Takayama K, Virgili F and Packer L. Nitric oxide synthesis and TNF-alpha secretion in RAW 264.7 macrophages, mode of action of a fermented papaya preparation, *Life Sci,* 67(6), 2000, 679-694.
24. Roche. Roto-granulations and taste masking coatings for preparation of chewable pharmaceutical tablets, US Patent 5 260 072 9, 1993.
25. Solanki H K, Bosuri T, Thakkar J H, Patel C A. Recent Advances in granulation technology, *International Journal of Pharmaceutical Sciences Review and Research,* 5(3), 2010, 48-49.
26. Sundaresan A, Niveditha R, Padmanabhan S, Hari B N V and Ramyadevi D. Oro-dissolving systems of papaya extract – liquisolid compacts and lozenges, *Int J Pharm Tech Res,* 6(7), 2014, 2083-2091.
27. Surbhi G, Seema S, Singh G, Rana A C. Industrial Process Validation of Tablet Dosage Form: An Overview, *International Research Journal of Pharmacy,* 3(3), 2012, 49-51.
28. Udaykumar M, Nageswarao A B N, Kumar V T V S, Giri V V. Fast Dissolving Tablets: New Fangled Drug Delivery System, A Comprehensive Review, *International Journal of Research in Drug Delivery,* 2(3), 2012, 15-25.
29. Wilson R K, Kwangyamdsorgergj. Effects of papaya seed extract and benzyl isothiocyanate on vascular contraction, *Life Sci,* 71(5), 2002, 235-239.
30. Yasir M. Formulation and evaluation of chewable modified release tablet containing sodium fluoride and vitamin, *Int J Pure Appl Biosci,* 3(2), 2015, 95-104.

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