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Research Article

DESIGN AND CHARACTERIZATION OF TRAMADOL HCL MEDICATED HARD LOLLIPOPS

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ABSTRACT

The oral route is the most preferred route of administration of drug because low cost of therapy. Ease of administration, patient compliance and flexibility in formulation. The illness are associated with fever headache and body aches so to cure the above/relief from the above, there was need to administer the drug to the individuals but in case of pediatric patients it was difficult to administer the dose forms like tablet, capsule, etc. In the present investigation, an attempt has been made to prepare and evaluate the sugar based tramadol hydrochloride medicated lollipops for pediatrics to overcome the administration. They were prepared by heating on congealing method on laboratory scale with sugar syrup as base. All the formations were subjected to various physico chemical parameter such as hardness, friability, content uniformity, Wight variation, thickness, drug content and in vitro dissolution studies. Drug excipients compability studies were conducted by FT- IR spectroscopy and result release studies showed that formulations F15 release the drug 89.41 percentage at the end of 30 min. The medicated lollipops can provide an attractive alternative formulation in the treatment of pain in pediatric patient.

Keywords: Tramadol Hydrochloride, FTIR, heating congealing method.

INTRODUCTION

In oral drug delivery, there are voluminous scientific tasks that could be studied for years to originate and innovation technologies are required to engender novel dosage forms raising drug delivery to higher level. This object examines quite a few in oral drug delivery necessitating implementation of novel ideas to improve oral drug delivery systems. Drug delivery is an escalating field that represents one of the foremost research and development concentration areas of pharmaceutical industry today, with new drug delivery system sales exceeding 10 billion dollars per year.

MEDICATED LOLLIPOPS

A small and medicated candy intended to be dissolved slowly in the mouth to lubricant and so that irritated tissues of the tract. A small flavoured tablet made sugar (or) syrup and often medicated. A small medicinal tablet initially in the shape of lollipops, taken for sore throat and dissolved in the mouth.

Lollipops are large sugar boiled confectionary of various flavours attached to a plastic stick which can be consumed over a long period of time through licking. The plastic stick is used to hold the confection together.

Lollipops are the dosage forms that dissolve slowly on the mouth (or) that can be easily swallowed are gaining in popularity and especially among paediatric patients.

ADVANTAGES OF MEDICATED LOLLIPOPS

- Keeping the drugs in contact with the oral cavity for an extended period of time
- Having formulas that are easy to change and can be patient specific
- Lollipops can be given to those patients who have difficulty in swallowing
- Lollipops has a pleasant taste and it extends the time that a quantity of drug remains in the oral cavity to produce a therapeutic effect also pharmacist can prepare lollipops extemporaneously with minimal equipment and time
- Lollipops extends the time of drug in oral cavity to elicit a specific effect
- Lollipops are early to prepare with minimum amount of equipment and time
- Do not require water intake for administration. Technique is non-invasive and it is the case with parenteral

DISADVANTAGES OF MEDICATED LOLLIPOPS

- Heat labile drugs cannot be used in this formulation because of the high temperatures required for preparation.
- Drugs having minimum bitter taste are suitable.
- Heat stable drugs are suitable

MATERIALS AND METHODS

Tramadol Hcl, Sucrose, corn syrup, HPMC-3000cps, NaCMC, citric acid, calcium carbonate

PREFORMULATION STUDIES

1. Physical characterization of drug.
2. Analytical method development of drug.
3. Drug identification

Analytical Method Development

Calibration of Tramadol hydrochloride in pH 6.8 phosphate buffer

Preparation of pH 6.8 phosphate buffer

Weighed quantity of 28.80 gms of disodium hydrogen phosphate and 11.45 gms of potassium disodium phosphate were dissolved in sufficient distilled water and these make up to 1000 ml by using distilled water.

Determination of Absorption maxima (λ max) for Tramadol Hydrochloride

Standard stock solution of concentration of 1 mg/ml solution was prepared. From that stock, different aliquots were taken and diluted to 10 ml dark pH 6.8 phosphate buffer to obtain series of concentrations. The solutions were scanned on spectrophotometer in the UV range 200-400 nm. The graph indicates that the maximum absorbance is observed at 271 nm and it is the λ max of Tramadol Hydrochloride.

Linearity of Tramadol Hydrochloride in Phosphate buffer pH 6.8

1.Prepare primary stock solution by taking 10 mg of drug and by dissolving it in 10 ml of phosphate buffer pH 6.8 and prepare 1 mg/ml solution.

2.From the primary stock solution secondary stock solution was prepared of 100 µg/ml.

3.From the secondary stock solution further concentration of the absorbance of those dilutions was measured at 271 nm.

Table 1: Linearity of Tramadol Hydrochloride in Phosphate buffer pH 6.8

Concentration (µgm/ml)	Absorbance (nm)
10	0.062
20	0.112
30	0.168
40	0.224
50	0.275
60	0.348
70	0.412
80	0.465
90	0.526
100	0.562

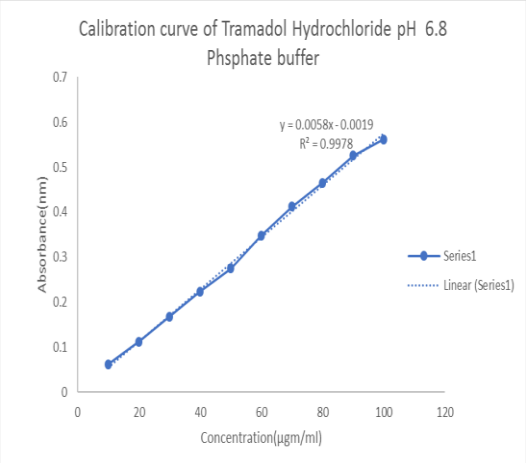

Fig. 1: Calibration curve of Tramadol hydrochloride pH 6.8 Phosphate buffer

Fourier Transforms Infrared Spectroscopy (FTIR)

Infrared spectrum of pure drug was recorded by using Bruker alpha-FTIR spectrophotometer.

FTIR was a sampling technique used in conjunction with infrared spectroscopy which enables samples to be examined directly in the solid state without further preparation.
In this, enough samples were placed on crystal area and the pressure arm was positioned over the sample area.
Force applied to the sample pushing it on to the surface.
Later the sample was analysed. The IR spectrum of pure Tramadol Hydrochloride was given in the figure.

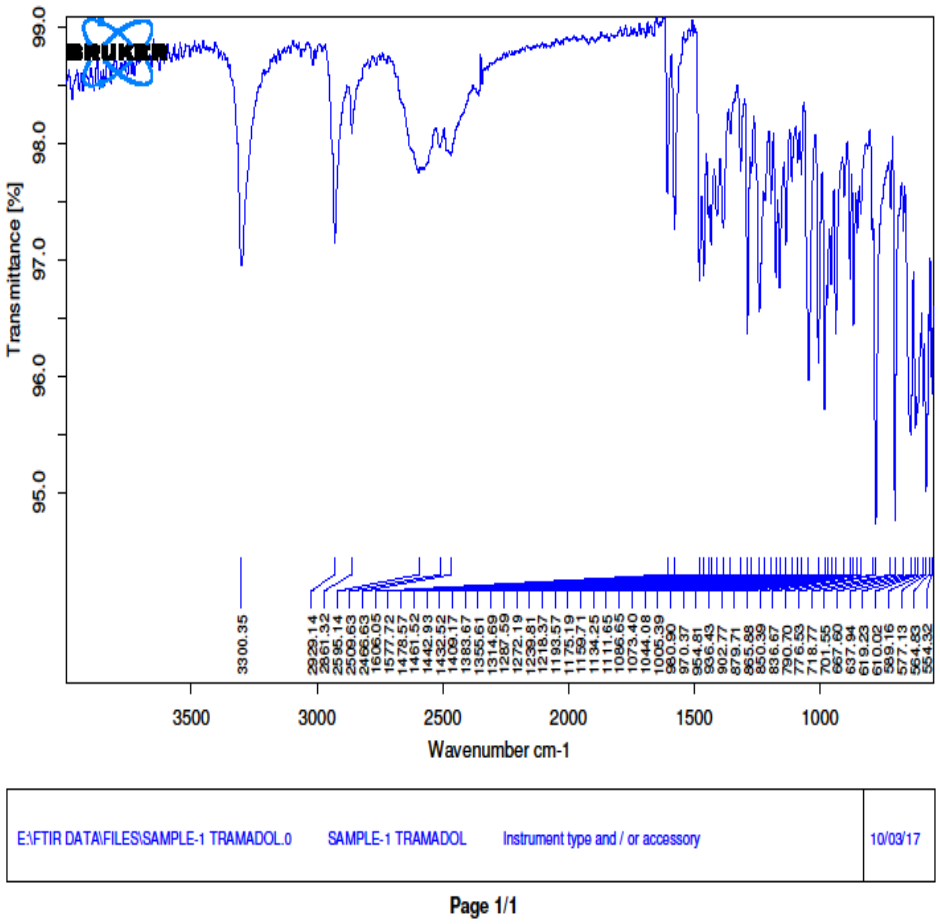

Fig. 2: FTIR peek Tramadol hydrochloride

IR INTERPRETATION

The different functional groups stretching's of pure drug were identified and in the spectra of drug with excipients these stretching's were reproduced and no new peaks were observed indicating there is no interaction of the drug with excipients. IR interpretation of pure drug and excipients was explained in the table.

Table 2: Interpretation of Tramadol hydrochloride

S.NO	FUNCTIONAL GROUP	INTERPRETATION VALUE	STANDARED VALUE
1.	N-H(S)	3300	3000-3700
2.	C-H(S)	2961	2960-2850
3.	C=C(S)	1461	1450-1600
4.	C-O(S)	936	900-1300
5.	C-N(S)	1044	1000-1410
6.	C-C(S)	836	800-1200

FORMULATION

Tramadol Hydrochloride Lollipops are prepared by heating and congealing method.

Heating and Congealing Technique

Tramadol Hydrochloride lollipops were prepared by heating and congealing technique.

1. Syrup base to be prepared by dissolving the required amount of sugar by heating at 110^{o}C for about 90 minutes.
2. Addition of base syrup by rising the temperature to 160^{o}C.
3. Cooling to obtain the plastic mass.
4. Addition of drug, polymer, colour and flavour with mixing.
5. Size roping of the materials in a moving roller after drying.
6. Wrapping with Polyethylene wraps.

Table 3: Formulation table of Tramadol Hydrochloride Hard Medicated lollipops F_{11} – $F1_5$

COMPOSITION	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}
Tramadol Hydrochloride (mg)	50	50	50	50	50
Sucrose (mg)	3395	3295	3195	3095	2995
Dextrose (mg)	-	-	-	-	-
Corn syrup (mg)	1400	1400	1400	1400	1400
Sodium CMC (mg)	100	200	300	400	500
HPMC3000cps (mg)	-	-	-	-	-
Citric acid (mg)	50	50	50	50	50
Calcium carbonate (mg)	5	5	5	5	5
Colouring agent	Q. S	Q. S	Q. S	Q. S	Q. S
Flavouring agent	Q. S	Q. S	Q. S	Q. S	Q. S
Total weight(mg)	5000	5000	5000	5000	5000

Table 4: Formulation table of Tramadol Hydrochloride Hard Medicated lollipops F_{16} – F_{20}

COMPOSITION	F_{16}	F_{17}	F_{18}	F_{19}	F_{20}
Tramadol Hydrochloride (mg)	50	50	50	50	50
Sucrose (mg)	-	-	-	-	-
Dextrose (mg)	3395	3295	3195	3095	2995
Corn syrup (mg)	1400	1400	1400	1400	1400
Sodium CMC (mg)	-	-	-	-	-
HPMC 3000cps(mg)	100	200	300	400	500
Citric acid (mg)	50	50	50	50	50
Calcium carbonate (mg)	5	5	5	5	5
Colouring agent	Q. S	Q. S	Q. S	Q. S	Q. S
Flavouring agent	Q. S	Q. S	Q. S	Q. S	Q. S
Total weight(mg)	5000	5000	5000	5000	5000

EVALUATION STUDIES

Evaluation of physical properties of medicated lollipops

The formulated lollipops and tablets were evaluated for the following parameters.

1. THICKNESS

The thickness and diameter of the formulated lollipops were measured by using Vernier callipers.

2. WEIGHT VARIATION

The formulated lollipops were tested for weight uniformity. 20 tablets were collectively and individually. From the collective weight, average weight was calculated. Each lollipop weight was then compared with average weight to ascertain whether it is with in permissible limits or not.

% Weight Variation =

$$\frac{\text{Average weight-Individual weight}}{\text{Average weight}} \times 100 \quad (1)$$

3. HARDNESS

The lollipops crushing strength, which is the force required to break the lollipop by compression in the diametric direction was

measured in triplicate using Pfizer tablet hardness tester.

4. FRIABILITY

The Roche friability test apparatus was used to determine the friability of the lollipops. 5 pre-weighed lollipops were placed in the apparatus, which was subjected to 100 revolutions. Then the lollipops were reweighed. The percentage friability calculated was using the formula.

% Friability =

$$\frac{\text{Initial weight- Final weight}}{\text{Initial weight}} \times 100 \quad (2)$$

5. DRUG CONTENT

Lollipops were weighed and powdered. The quantity of powder equivalent to 100 mg of Tramadol Hydrochloride was dissolved in 7.4 pH phosphate buffer diluted to 100ml with7.4 pH phosphate buffer then the solution was filtered and suitably diluted. The drug content was estimated spectrometric ally at 271 nm.

6. *IN-VITRO* DISSOLUTION STUDIES:

Dissolution rate was studied using USP-II paddle dissolution apparatus, in 900ml of Tramadol Hydrochloride 37±0.5°at 100 rpm. Aliquot of dissolution medium was withdrawn at regular time intervals and the same volume of pre-warmed (37±0.5°) fresh dissolution medium was replaced. The samples were filtered and drug content of Tramadol Hydrochloride in each sample was analyzed after suitable Dilution by Shimadzu UV-spectrophotometer at 271 nm.

RESULTS

EVALUATION RESULTS

Table 5: Weight variation, Hardness, Diameter, Thickness, Friability and Drug content results F11-F20

Formulation code	Weight Variation (gm)±SD	Diameter (cm)	Thickness (mm)	Friability (%)	Hardness (kg/cm^2)	Drug content (%)
F11	5.01±1.03	2.73±0.0	7.09±1.05	0.92±0.01	10.86±0.01	58.62±0.31
F12	5.00±1.11	2.74±0.0	7.20±0.03	0.96±0.01	10.93±0.01	63.31±0.32
F13	5.03±0.62	2.70±0.0	7.24±0.03	0.94±0.01	11.02±0.01	68.41±0.32
F14	5.00±0.1	2.71±0.0	7.26±0.03	0.95±0.01	11.06±0.01	77.61±0.01
F15	5.03±1.04	2.70±0.0	7.30±0.03	0.95±0.01	11.08±0.05	89.41±1.09
F16	5.01±0.12	2.71±0.0	7.02±0.01	0.96±0.02	11.03±0.05	48.06±0.32
F17	5.02±0.12	2.72±0.0	7.14±0.04	0.95±0.02	11.01±0.01	65.64±0.01
F18	4.98±1.12	2.70±0.0	6.98±0.41	0.95±0.02	11.06±0.02	70.41±0.62
F19	4.96±0.21	2.70±0.0	7.12±0.01	0.94±0.01	11.04±0.01	73.41±0.6
F20	5.00±1.22	2.71±0.0	7.16±0.01	0.92±0.01	11.05±0.01	76.41±0.1

Table 6: In-vitro dissolution data of Tramadol Hydrochloride Hard Medicated Lollipops by using solid dispersion F11-F15

Time(min)	F11	F12	F13	F14	F15
0	0	0	0	0	0
5	10.31±1.32	13.31±4.1	17.41±0.3	19.41±0.82	21.32±1.42
10	17.41±6.3	21.61±0.41	23.31±2.01	25.41±2.01	39.40±1.02
15	28.31±0.31	30.41±2.01	37.41±0.41	39.31±1.01	48.31±2.01
20	34.61±0.41	37.31±1.01	40.41±6.21	48.41±6.2	62.41±3.2
25	49.61±3.21	52.41±6.62	60.31±0.01	68.41±1.2	74.81±2.6
30	58.62±0.31	63.31±0.32	68.41±0.32	78.61±0.01	89.41±1.09

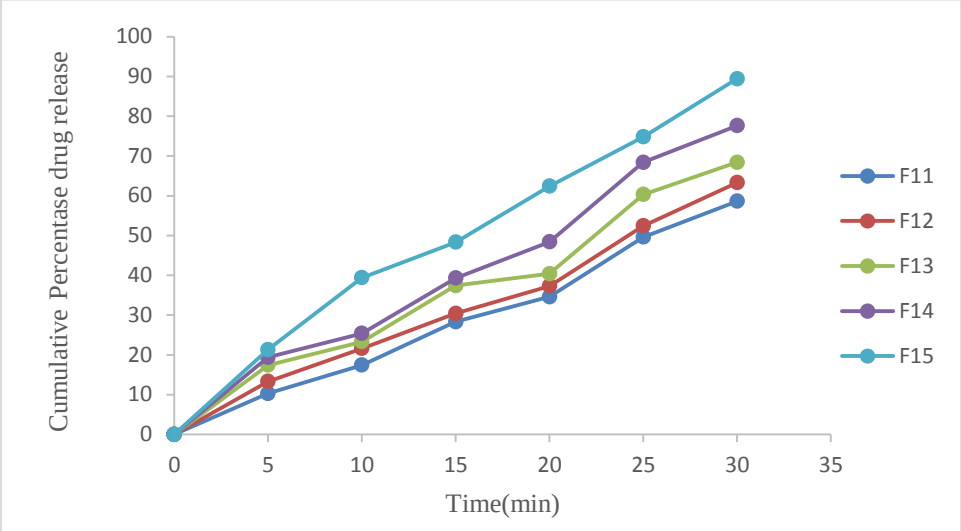

Fig. 3: In vitro drug release kinetic graph of formulations F11-F15

Table 7: In-vitro dissolution data of Tramadol Hydrochloride Hard Medicated Lollipops by using solid dispersion F16-F20

Time(min)	F16	F17	F18	F19	F20
0	0	0	0	0	0
5	9.41±6.32	12.41±0.63	18.31±5.5	20.21±6.1	28.43±0.21
10	18.41±0.32	23.06±2.31	30.31±2.1	35.41±6.1	40.31±3.1
15	24.01±6.32	37.41±1.22	39.61±4.1	43.21±6.2	52.31±5.1
20	33.01±2.41	40.41±6.32	48.62±3.21	54.81±0.2	59.41±1.03
25	39.31±1.32	50.62±2.31	58.64±0.32	67.41±0.2	63.82±7.3
30	48.06±0.32	65.64±0.01	70.41±0.62	73.41±0.6	76.41±0.1

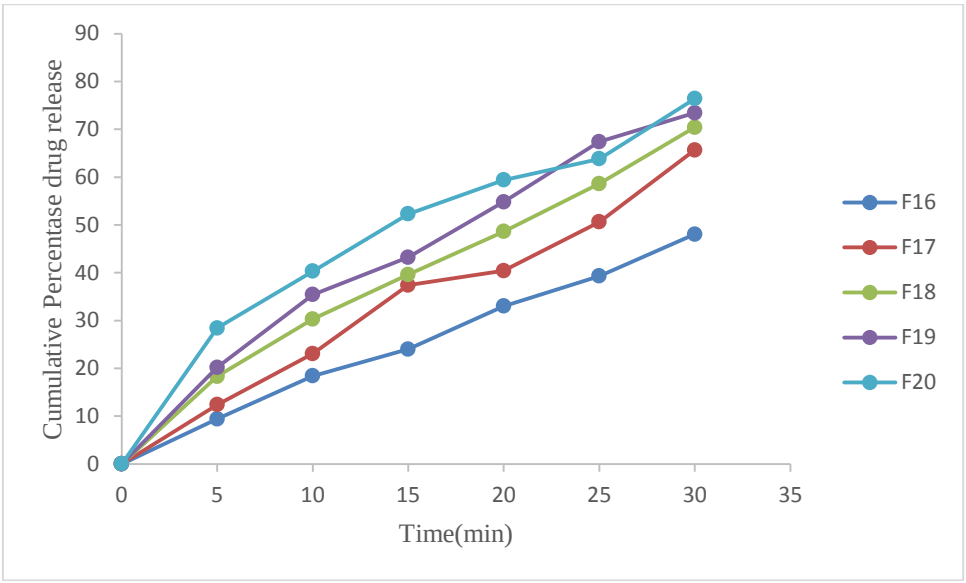

Fig. 4: In vitro drug release kinetic graph of formulations F16-F20

CONCLUSION

From the present study it was suggested that corn syrup based tramadol hydrochloride wiil be ideal dosage forms for the treatment of pain to the paediatrics. By incorporation of synthetic polymers yields good results and release the drugs for a prolonged period of 30 mins.

Lollipops are intented to slowly dissolve in the mouth over a relatively long period of time. Eg; usually about 2-15 mins or more as needed. The taste bud and olfactory sences are able to

detect even the slightest bittetness of unpleasant mouth feel and taste during such a long residence time in the mouth represents a substantial challenges it is desirable to provide a palatable dosage form of tramadol hydrochloride hard lollipops

REFERENCES

1. Rao TV, Bhadramma N and Kinnera K. Design and development of Tramadol Hydrochloride Lozenges for the treatment of pain in paediatrics. International Journal of general pediatrics and medicine. 2016;23-32.
2. Renuka P, Shayeda, Madhusudan Rao Yamsani. Development and In-vitro Evaluation of Nicotine Hard Candy Lozenges for smoking cessation International Journal of pharmacy and pharmaceutical sciences. 2014;6(2):0975-1491.
3. Deepika modyala, Aparna C and Prathima Srinivas. Formulation, evaluation and characterization of Itraconazole Lozenges, ISOR Journal of pharmacy and Biological sciences. 2014; 9(1):86-94.
4. Dasharath M Patel, Rahul J Patel, Hardik R Shah and chhagan N Patel. Formulation and Evaluation of Diphenhydramine Hydrochloride Lozenges for treatment of cough. World Journal of pharmacy and pharmaceutical sciences. 2014;3(5):822- 834.
5. Kirit Sondarva and sulekha Bhadra. Development of Cefixime lozenge for the treatment of Throat Infection. World Journal of pharmacy and pharmaceutical sciences. 2015;4(7):645-656.
6. Srikanth Parepalli, Madhusudan Rao Y and Shravan Kumar Y. Formulation and Evaluation of Levodropropizine Lozenges. World Journal of pharmaceutical Research. 2015;4(4):646-659.
7. Rohan Patil, Neha Patil, Shid SJ, Dange VN, Magdum CS and Mohite SK. Preparation and Evaluation of Fast Dissolving Tablet Tramadol. Asian Journal of pharmaceutical and Clinical Research. 2016;6(3).
8. Pundir S and Verma AM. Formulation Development and Evaluation of Antiemetic Lozenges of Ondansetron hydrochloride. International Journal of Research in Medical and health sciences. 2013;2(4).
9. Purushotham Rao K, Girish Ktti, Ajay Kartik and Manjunath P. Design of Medicated Lozenges for Pediatrics. International Journal of Research in Medical and health sciences. 2013;2(4).
10. Sonali J Shah and Rupa Muzumder. Formulation Development and Evaluation of Mouth Dissolving Tablet of Tramadol hydrochloride. Asian Journal of pharmaceutical and Clinical Research. 2013;6(3).
11. Sarinder Kakar, Ranadeep Singh and Manisha Shah. Formulation and Evaluation of Orodispersible Tablets of Tramadol hydrochloride. FARAD Journal of pharmaceutical sciences. 2013;32(2):73-81.
12. Nagaba Shivappa N, Purushotham Rao K and Zakaullah S. Formulation of Clotrimazole as Lozenge Tablet for Improved delivery to Oral Thrush. Journal of pharmaceutical and Biomedical Sciences. 2011;12(17).
13. Jayalakshmi Kamath, Dungrani Jayesh and Johnson Misquith. Preparation and In-vitro Evaluation of Levamisole hydrochloride as a candy Based Anthelmintic Medicated lollipops for Pediatrics. International Journal of pharma science and Research. 2012;3(11).
14. Venkateswara Rao T, Bhadramma N and Kinnera K. Design and In vitro Evaluation studies of Tramadol Hydrochloride Lozenges for treatment of pain in Children. Science Innovation 2015;3(6):100-107.
15. Madhusudan Rao Yamsani, Shravan Kumar Y and Sandeep P. Formulation and evaluation of Lidocaine Lozenges. International Journal of Innovative Research in Sciences, Engineering and Technology. 2015;4(11).
16. Syed wajid, Mohamed N Al-Arief and Suhair S Al Saleh. Design and Evaluation of orally Disintegrating Tramadol Hydrochloride Tablets by Direct Compression method. British Journal of pharmaceutical Research. 2015;8(4):1-8.