Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 07, 2023

Original Research

Comparative Study Between Natural And Synthetic Polymers On Drug Release Of Sustain Release Matrix Tablets Of Nevirapine

Sk. Irfan Khan[1]*, Sk. Waseem Uddin[2], Velisetty Alekya[3], Anurag Rai[4], J. Satya Sri[5], Shaik Shabbeer[6], K. N. V. Rao[7].

[1]*, 2, 3, 4,5,6,7 Department of pharmaceutics, Nalanda college of pharmacy, Telangana, 508001

***Corresponding Author:** SK. Irfan Khan
*Associate professor, Department of pharmaceutics, Nalanda college of pharmacy, Telangana, 508001, Email: Ikhanu65@gmail.com

ABSTRACT
The aim of present investigation was to develop sustain release matrix tablets for sustain release drug delivery of nevirapine. The medication used for the treatment of HIV infected patients. The drug delivery system was designed to deliver the drug for such a time when it could be needed for patient conditions. The sustain release matrix tablets containing nevirapine in the inner core were formulated by direct compression method with an outer coating of different concentration of natural and synthetic polymers (HPMC, MCC, PECTIN). The release profile of sustain release matrix tablets exhibited a lag time. The optimized batch F5 gave good disintegration & dissolution of percentage drug release of tablet. So, on this basis we have concluded that the F5 formulation containing the pectin 50mg which is going to be selected as best formulation.

Keywords: nevirapine, pectin, HPMC K100M, MCC and direct compression method

INTRODUCTION

The term “sustained release” is known to have existence in the medical and pharmaceutical literature for many decades. It has been constantly used to describe a pharmaceutical dosage form formulated to retard the release of a therapeutic agent such that its appearance in the systemic circulation is delayed and/or prolonged and its plasma profile sustained in duration. The onset of its pharmacological action is often delayed and the duration of its therapeutic effect is sustained. One of the least complicated approaches to the manufacture of sustained release dosage forms involves the direct compression of blend of drug, retardant material and additives to formulate a tablet in which the drug is embedded in a matrix of the retardant. The materials most widely used in preparing matrix system include both hydrophilic and hydrophobic polymers. Commonly available hydrophilic polymers include hydroxypropyl methyl cellulose (HPMC), Hydroxypropyl cellulose (HPC), Hydroxyethyl cellulose (HEC), Xanthan gum, Sodium alginate, Poly (ethylene oxide) and cross linked homopolymers and copolymers of acrylic acid. It is usually supplied in micronized forms because small particle size is critical to the rapid formation of gelatinous layer on the tablet surface.
Ideally a sustained release oral dosage form is designed to release rapidly some loading dose of drug, which will produce the desired pharmacological response as promptly as possible and the maintenance dose is then released at constant rate.The rate of drug absorption from the entire maintenance dose into the body should be equal to the rate of the drug removal from the body by all the processes over the time of which the desired intensity of the pharmacological response is required.

The main effort to suppress transmission of HIV has focused on targeted inhibition of reverse transcriptase (RT) and other enzymes of viral replication. Nevirapine, a dipyridodiazepinone, is a representative of a new class of anti-HIV agents, the non-nucleoside RT inhibitors. This orally administered agent is currently in late phase clinical studies in several European countries, Australia, South Africa and Canada. In common with a number of other anti-HIV agents, it has received accelerated approval in the US.

Nevirapine is an important NNRTI (non-nucleoside reverse transcriptase inhibitor) class of anti-retroviral drug acting through inhibition of HIV-1 reverse transcriptase enzyme subsequently causing stoppage of viral replication. A study conducted on comparison of nevirapine SR formulation versus nevirapine immediate release in treatment navirapine patients, it was found that define sustained release formulations dosed once daily has more clinical efficacy than nevirapine immediate release formulation dosed twice daily. Hence nevirapine can be suitably formulated as a sustain release matrix tablets owning to its high clinical efficacy when compared to nevirapine immediate release formulation.

MATERIALS AND METHODS

Materials: Nevirapine was procured from SYN Pharma Pvt. Ltd, HPMC, MCC, Lactose, Starch, talc, magnesium stearate were of laboratory grade. Orange fruits were obtained from the local market.

Extraction of Pectin:

1. Selection of citrus fruit for extraction of pectin that is (orange).
2. 500 gm of orange peel is taken and dried for four days.
3. After drying converted into the powder form.
4. For extraction process take total of 50ml HCL and 5 litre distilled water in 5 different beakers.
5. After mixing keep it for 24 hrs.
6. The 1 litre of filtrate is added to 1 litre ethanol (95%) to each beaker.
7. This mixture is kept in centrifugation apparatus.
8. After that left for 1 hr and filtered through Buchner funnel.
9. Add some known quantity of acidified ethanol to residue.
10. Wash the filtrate with 250 ml of acetone and dried it at room temperature for one day.
11. The dried product is grind into fine powder and sieved by 40 – 42 mesh sieve to separate pectin from fibre.
12. The pectin powder is then collected and weighed.

Formulation of nevirapine sustained release matrix tablets

Nevirapine sustained release matrix tablets were prepared by direct compression method employing starch as binder, pectin as a retarding polymer, lactose as diluent. Six formulations of tablets each containing 500mg dose of nevirapine were prepared with different concentrations of various excipients which were shown in table 1.

Nevirapine and polymers such as pectin, HPMC, MCC and other ingredients were accurately weighed and passed through the sieve # 40 and all the materials were taken in mortar and pestle mixed for 10 min. magnesium stearate was passed through the sieve #60 mixed together with mixture in mortar and pestle for 5 min to get uniform blend and the mixture was compressed in to tablets using rotary tablet compression machine.

INGREDIENTS	F1	F2	F3	F4	F5	F6
Drug	200	200	200	200	200	200
Hydroxypropyl methyl cellulose	50					

Micro crystalline cellulose			50	100		
Pectin					50	100
Lactose	200	150	200	150	200	150
Starch	48	48	48	48	48	48
Magnesium stearate	1	1	1	1	1	1
Talc	1	1	1	1	1	1

Table- 1: composition of different formulation from F1 to F6

Evaluation of sustained release matrix tablets Angle Of Repose

The internal angle between the surface of the pile of blend and the horizontal surface is known as the angle of repose.

Method

The blend was passed through a funnel fixed to a burette stand at a height of 4 cm. A graph paper was placed below the funnel on the table. The height and radius of the pile was measured. Angle of repose of the blend was calculated using the formula:

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

Where,

h = Height of the pile r

= Radius of the pile

Bulk density

The bulk density is used as a measure to describe packing materials or granules.

Method

Bulk density is the ratio of given mass of powder and its bulk volume. It was determined by transferring an accurately weighed amount (25 gms) of powder sample to the graduated cylinder with the aid of a funnel. The initial volume was noted. Ratio of weight of the sample to the volume it occupied was calculated.

$$\text{Bulk density} = W/V_0 \text{ g/ml}$$

Where,

W = Mass of the blend

V0 = Untapped volume

Tapped density Method

It was measured by transferring a known quantity (25 gms) of blend into a graduated cylinder and was placed on the tapped density apparatus. The initial volume was noted. The apparatus was set for 500, 750 and 1250 taps. The tapped density was determined as the ratio of mass of the blend to the tapped volume.

$$\text{Tapped density} = W/V_f \text{ g/ml}$$

Where,

W= Mass of the blend

Vf = tapped volume

Compressibility index

It is the propensity of a powder to be compressed.

Method

It is measured by tapped density apparatus for 500, 750 and 1250 taps for which the difference should be not more than 2 %. Based on the apparent bulk density and tapped density the percentage compressibility of the blend was determined using the following formula.

Compressibility index= [(V0 – Vf) / V0] X 100 (or)

% Compressibility= [(Tapped density – Bulk density) / Tapped density] X 100 /Tapped density

Hausner ratio

It indicates the flow properties of the powder. The ratio of tapped density to the bulk density of the powder is called Hausner ratio.

Hausner ratio = Tapped density/ Bulk density

POST COMPRESSION PARAMETERS

The compressed tablets were evaluated for the following parameters.

Weight variation test

Twenty tablets were selected at random and its individual weight was noted and from that, the mean weight of the tablets was calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage deviation and none should deviate by more than twice that percentage.

Hardness test

Tablet requires a certain amount of mechanical strength to withstand the shock of handling in its manufacture, packaging, shipping and dispensing. It may be especially important to monitor the tablet hardness for sustained release drug products or other products that possess real or potential bioavailability problems or sensitive to variations in drug release profile. The crushing strength that just causes the tablet to break is recorded by means of Monsanto hardness tester. The tablet is placed vertically in between the lower and upper plungers. The initial reading was taken immediately after placing the tablet onto the lower plunger. The upper plunger was then forced against a spring by turning a threaded bolt until the tablet gets fractured. As the spring was compressed, a point moves along a gauge in the barrel to indicate pressure. The position of the pointer at the time of tablet fracture was noted and the difference between the initial and the final readings was noted as hardness of the tablet. The value was expressed in Kg/cm2

Thickness

The thickness of the individual tablets was measured by using Vernier calliper and average thickness is determined. The thickness was denoted in millimetre.

Friability

Friability is the measure of tablet's ability to withstand both shock and abrasion without crumbling during manufacturing, packing, shipping and consumer use. Tablets that tend to powder, chip and fragment when handled lack elegance and hence consumer acceptance. The weight of 10 tablets was noted and placed in Roche friabilator. The device subjects the tablets to the combined effect of shock and abrasion by utilizing a plastic chamber which revolves at 25 rpm, rolling the tablets a distance of 6 inches with the revolution. The tablets were removed after 100 revolutions, dedusted and reweighed. Tablets that loose less than 0.5 to 1 percent in weight are generally acceptable. The percentage friability of the tablets were calculated by the formula.

$$\text{Percentage Friability} = \frac{\textit{Initial Weigh t} - \textit{FinalWeigh t}}{\textit{Initial Weigh t}} X\ 100$$

WETTING TIME AND WATER ABSORPTION RATIO

A piece of tissue paper folded twice was placed in a small petri dish of 6.5cm in diameter containing 6ml of water. A reweighed tablet was placed on the surface of tissue paper and allowed to completely wet. The time required for water to reach the upper surface of the tablet and to completely wet it was noted as the wetting time. The wetted tablet was then weighed. Water absorption ratio (R) was determined using the following equation,

$$R = \frac{Wa - Wb}{Wb} X\ 100$$

Where,
Wb - Weight of tablet before wetting.
Wa - Weight of tablet after wetting.

Disintegration test

Disintegration test was carried out at 370C±20C in 900 ml of distilled water stimulated gastric fluid or stimulated intestinal fluid. The disintegration time of tablets from each formulation were determined using disintegration test apparatus. One tablet was placed in each of the six tubes of the apparatus containing distilled water. One disk was added to each tube. The time taken in seconds for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured.

Dissolution In vitro dissolution studies

Dissolution Parameters Apparatus : USP Dissolution apparatus, type I [Basket]

Medium	: 900 ml of 0.1 M Hydrochloric acid
RPM	: 50 Temperature : 37°C ± 0.5°C
Sampling interval	: 5, 10, 15, 20, 25, 30, 45, 60. Minutes
Sample withdrawn	: 10ml
Wavelength	: 230nm
Instrument	: UV spectroscopy

Preparation of 0.1 M Hydrochloric Acid

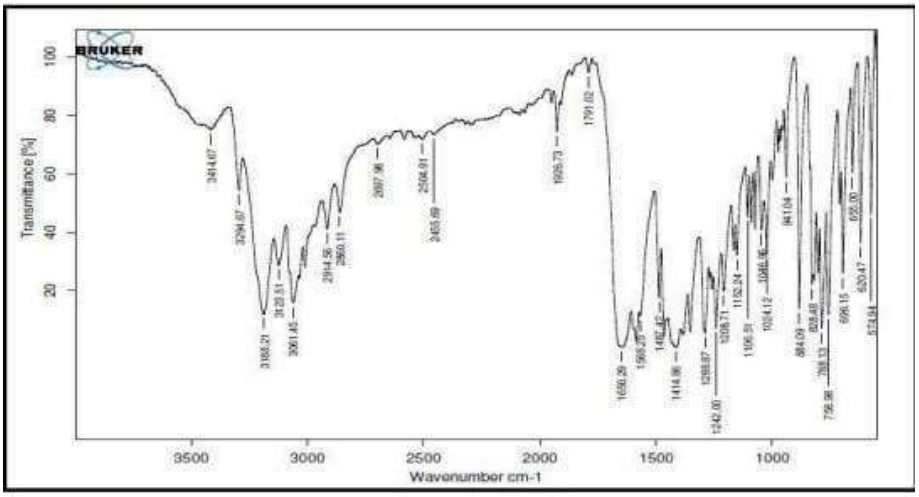
Place 8.5 ml of concentrated hydrochloric acid into the 1000 ml volumetric flask and the volume were made up with de-mineralized water.

Procedure

The in vitro dissolution studies of nevirapine sustained release matrix tablets were performed using USP dissolution apparatus type 1(basket). The volume of dissolution medium (0.1M HCl) used was 900 ml and the temperature was maintained at 37°C±0.5°C. The speed of the basket was set at 50rpm. One tablet was placed in each jar of dissolution apparatus. 10ml of sample from each jar was withdrawn at every 5minutes interval up to 10 minutes and same volume of 0.1M HCl was replaced to each dissolution jar, so that volume of dissolution medium was maintained to 900ml. Then the sample was filtered and diluted with 0.1M HCl and the amount of nevirapine released from SRMTS was determined spectrophoto metrically at 230 nm using 0.1M HCl as blank.

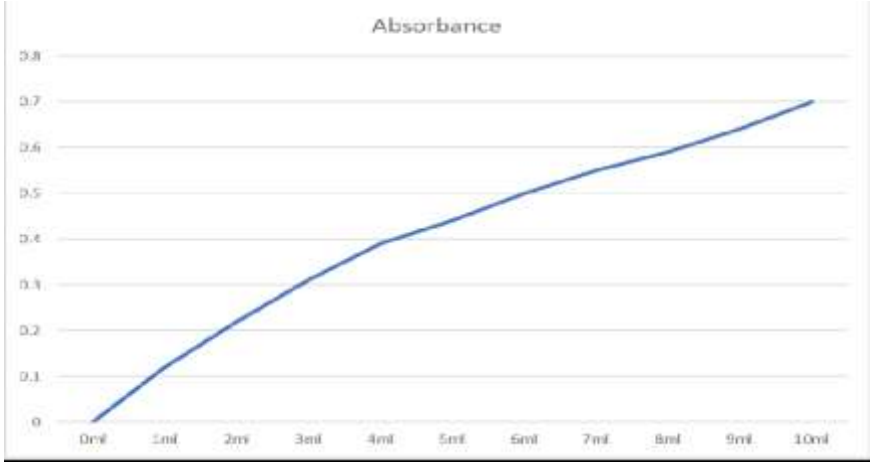
RESULTS AND DISCUSSION

The present study was undertaken to formulate nevirapine sustain release matrix tablets. This study involves preformulation studies of drug and excipients, formulation and processing development along with evaluation of tablets made with the optimised formulation. Nevirapine were successfully developed in order to sustain the drug release rate by pectin as a release retarding polymer.
FTIR of pure Nevirapine: FTIR of nevirapine exhibits characteristic peaks for amide group at 3188.21cm-1 and 1650.29 cm-1 due to N-H and C=O stretching respectively, at 3061.45 cm-1 (C-H stretch, pyridines), 1288.87 cm-1 (Aromatic amine group, C-N stretch).



STANDARD GRAPH/CALIBRATION CURVE

10 ml of stock solution was made to 100 ml with 0.1N HCl, it gives a concentration of 100µg/ml. Aliquots of standard drug solution ranging from 0.1, 0.2, 0.4, 0.6, 1.2, 2.0 ml were transferred in to 10 ml volumetric flask and were diluted up to the mark with 0.1N HCl. Thus, final concentration ranges from 1, 2, 4, 6, 12, 20 µg/ml. Absorbance of each solution was measured at 230 nm against 0.1 N HCl as a blank. A plot of concentration of drug vs absorbance was plotted. The linear regression analysis was done on absorbance data points. A straightline equation was generated to facilitate the calculation of amount of the drug. The equation is as follows
Y=mx+c
Where, Y=
absorbance, m=
slope, x=
concentration, c=
intercept



PREFORMULATION PARAMETERS

Formulations	Angle of repose	Bulk density	Tapped density	Carr's index
F1	36.12	0.48	0.61	27.8
F2	38.65	0.48	0.53	10.4
F3	36.86	0.44	0.61	38.63
F4	37.95	0.48	0.60	25
F5	34.75	0.53	0.68	28.3
F6	37.69	0.47	0.59	25.53

Table: 2 Preformulation Parameters.

POST FORMULATION PARAMETERS

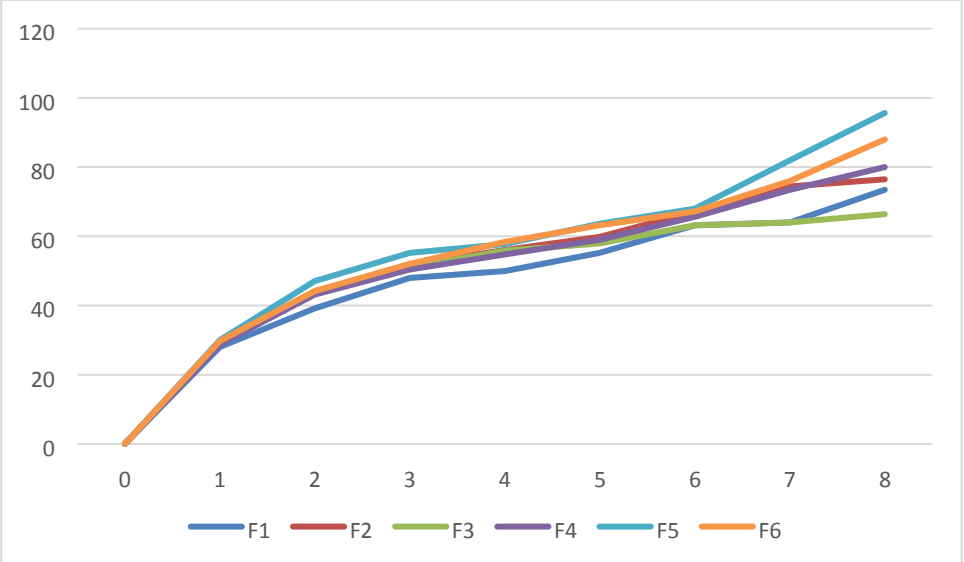
Formulation Code	Average weight mg)	Thickness (mm)	Hardness (kg/cm^2) Percentage	Friability (%)	Disintegration Time (sec)	Wetting time (sec)
F1	0.494	0.6	4.5	17.02	1:40	1:00
F2	0.504	0.6	4.5	10.78	25	1:30
F3	0.500	0.6	2.5	38.94	1:24	52
F4	0.500	0.6	5.5	10.78	17	56
F5	0.504	0.6	4.5	24.66	15	1:05
F6	0.500	0.6	4.5	23	18	1:00

Table: 3 Post formulation Parameters

DISSOLUTION TABLE

Time (min)	F1	F2	F3	F4	F5	F6
5	28.00	29.6	29.440	28.8	30.04	29.76
10	39.20	43.84	44.160	43.2	47.04	44.16
15	48.00	51.84	51.040	50.4	55.20	52
20	49.92	56	55.840	54.72	57.76	58.4
25	55.20	59.84	57.92	59.04	63.68	63.2
30	63.20	67.2	63.200	65.664	68.00	67.2
45	64.00	74.4	64.00	73.44	81.92	76
60	73.44	76.48	66.400	80	95.65	88

Table: 3 Values of dissolution studies



Percentage of drug release of nevirapine

CONCLUSION:

In this study sustain drug release matrix tablet dosage form was formulated by direct compression method. The lag time and time controlled release behaviour of nevirapine from sustain release matrix tablets could be modulated by varying the concentration of polymer in outer coating layer with the concentration of 50mg & 100mg of synthetic & natural polymers. F5 showed faster drug release than the other formulations. Faster drug release can be correlated with the less disintegration time & dissolution time. F5 formulation which contains the pectin 50mg which is selected as best formulation. Hence F5 Formulation was considered as optimized Formulation.

ACKNOWLEDGEMENT

The authors wish to thanks to management, principal of Nalanda college of pharmacy, Department of pharmaceutics and Jawaharlal Nehru Technological University, Hyderabad for providing facilities to carry out this work.

REFERENCES

1. **M. Sunitha Reddy et. al,** Formulation & evaluation of nevirapine sustained release matrix tablets using mucilage of ameimoschus esculents as release modifier, International journal of pharmacy and pharmaceutical science, Vol 6, Issue 5, NOVEMBER 2014, centre of pharmaceutical sciences &technology, Jawaharlal Nehru university, Kukatpally, Hyderabad, Telangana, India.

2. **P. R Radhika et. al,** Formulation and Evaluation of Sustained Release Matrix Tablets of Glipizide, Iranian Journal of Pharmaceutical Science, JUNE 2009: 5(4): 205-214 ijps.sums.ac.ir, Bioequivalence Study Centre, Department of Pharmaceutical Technology, Jadavpur University, Kolkata, India.

3. **Raghavendra Rao n. G et. al,** formulation and evaluation of sustained release matrix tablets of tramadol hydrochloride, International Journal of Pharmacy and Pharmaceutical Sciences, Vol. 1, Suppl 1, Nov.-Dec. 2009, PG Department of Pharmaceutics, Luqman College of Pharmacy, Old

Jewargi Road, Gulbarga - 585 102. 2 Department of Pharmaceutics, N.E.T. Pharmacy College, Raichur.

4. **Indranil Kumar Yadav et. al,** formulation, evaluation and optimization of aceclofenac sustained release matrix tablets, International Journal of PharmTech Research CODEN (USA): IJPRIF ISSN: 0974-4304 Vol.2, No.1, pp 592-598, Jan-Mar 2010.

5. **Arkhel Alka et. al,** Formulation development and evaluation of sustained release matrix tablet of Lamivudine using tamarind seed polysaccharide, Der Pharmacia Lettre, 2011, 3(3): 250-258, (School of Pharmaceutical Sciences, Rajiv Gandhi Proudyogiki Vishwavidyalaya, Bhopal, M.P., India. (http://scholarsresearchlibrary.com/archive.html),

6. **Syed Namath et. al,** Formulation and Evaluation of Sustained Release Matrix Tablets of Lornoxicam, International Journal of Drug Development & Research | Jan-March 2011 | Vol. 3 | Issue 1 | ISSN 0975-9344, Department of Industrial Pharmacy, Acharya & BM Reddy College of Pharmacy, Bangalore.

7. **G. Rajalakshmi et. al,** Formulation and evaluation of theophylline sustained release matrix tablet, Der Pharmacia Lettre, 2011, 3 (6):1-7, Department of Pharmaceutics, SRM College of Pharmacy, Kattankulathur, India. (http://scholarsresearchlibrary.com/archive.html),

8. **Mohd Abdul Hadi et. al,** Formulation and Evaluation of Sustained Release Matrix Tablets of Glimepiride Based on Combination of Hydrophilic and Hydrophobic Polymers, Journal of Applied Pharmaceutical Science 02 (06); 2012: 101-107, JUNE 2012, Dept of Pharmaceutics and Pharmaceutical Analysis, Bhaskar Pharmacy College, Yenkapally (V), Moinabad (M), R.R District, Hyderabad-500075, A.P, India.

9. **Dr. Ragavendra Kumar et.al**, Design and Formulation And In Vitro Evaluation of Sustained Release Matrix Tablets of Losartan Potassium, research article slide share, MAY 2017.

10. **M Vanaja Kumari et. al,** formulation and evaluation of sustained release matrix tablets of ranolazine, Vanaja, et al. Int J Pharm 2012; 2(1): 224-229 ISSN 2249-1848, Hetero drugs limited, Jeedimetla, Hyderabad-500055, India. Department of Pharmaceutics, Malla Reddy College of Pharmacy, Dulapally, Secunderabad, India.

11. **MadishNiaz**, slide share of nevirapine, NOVEMBER 2019.

12. **Roma Chaudhary et.al**, Formulation and In-Vitro Evaluation of Sustained Release Matrix Tablets of Domperidone, (2020) Vol.08 No.02 Issue 22, Department of Pharmacy, Universal College of Medical Sciences, Bhairahawa, Nepal (2020) Vol.08 No.02 Issue 22.

13. **Santhosh Kumar**, Formulation and Evaluation of Sustained Release Matrix Tablets, slide share DECEMBER 2014.

14. **Rupali et.al**, Formulation and Evaluation of Sustained Release Matrix Tablet of Simvastatin Using Synthetic Polymers, international journal of pharmacy and pharmaceutical research, NOVEMBER 2019 Vol.:16, Issue:4, Himalayan Institute of Pharmacy, Kala-Amb, Himachal Pradesh-173030, India.

15. **Frederick W.A. Owusu et.al**, Formulation and Evaluation of Sustained Release Matrix Tablets of Capparis Erythrocarpos Roots Extract To Improve Patient Compliance In Management Of Arthritis, Scientific African, SEPTEMBER 2019, department of Pharmaceutics, pharmacology, pharmacognosy Faculty of Pharmacy and Pharmaceutical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.