FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLET OF ANTIHYPERTENSIVE DRUGS ACCORDING TO BCS SYSTEM

***Abhijit Sonje[1], Arun Yadav[1], A. Chandra[2], D. A. Jain[3].**
[1]**Baxil Pharma Pvt Ltd, Nainital Highway, Shyampur, Dist-Haridwar 249 408 (India)**
[2]**Institute of Pharmacy, Amity University, Noida-201301, India.**
[3]**Institute of Pharmaceutical Science and Research Center, Bhagwant University, Ajmer, India.**

ABSTRACT

The main object of this study was to find out effect of two different lubricants at different concentrations (1% and 2%), of four different drugs. Four different drugs were selected according to Biopharmaceutical Classification System and their availability of antihypertensive drugs like Class 1- Propranolol Hcl, Class 2- Carvedilol, Class 3- Atenolol, and Class 4- Hydrochlorothiazide. From this study, it was revealed that, retardation of drug release increased as the concentration of lubricant increases. Sodium Stearyl Fumerate gives better result than Magnesium Stearate.

KEYWORDS : Lubricants, Biopharmaceutical Classification System, Antihypertensive Drugs.

INTRODUCTION

The oral route of drug administration is the most popular and successfully used conventional drug delivery dosage form. It offers the advantages of convenience. Ease of administration, Greater flexibility in dosage form design, Ease of production, and low cost. The parenteral route of administration is important in case of emergencies. While the topical route of drug administration is recently employed to deliver drug to the specific part of the body for systemic effect. It is probable that almost 90% of all the drugs are administered by oral route. [1]

The dosage forms available for oral administration are solution suspension, powders, tablets and capsules. The physical state of most of the drugs being solid and they are administered in solid dosage form. The drugs administered by oral route are versatile, flexible in strength, relatively stable, present less problem in formulation and packaging and are convenient to manufacturer, store, handle and use, Solid dosage forms provide best protection to drugs against temperature, light, oxygen and stress during transportation, Most employed solid oral dosage form are tablet and capsule. Tablet has number of advantages over capsule.[2]

The objective of the present study is to formulate and evaluate immediate release tablet according to Biophannaceutical Classification System (BCS) and compare the effect of lubricant on dissolution profile. Select the antihypertensive drugs according to the Biopharmaceutical Classification System (BCS). To prepare the immediate release tablets by using the different concentrations of the Lubricants. Compare the dissolution profile of all the trial batches formulated and select the best lubricant for the final formulation.

MATERIAL AND METHODS

In Vitro Dissolution Study [23]

In vitro dissolution studies were done with tablets in a following way:

Propranolol tablets [23]

1) Dissolution parameter [23]

Medium-Dilute Hydrochloric acid (1 in 1000ml)
Apparatus- USP-1 (Basket)
RPM-100
Time- 5,10,15,20,25,30 min.
Temperature- 37°C±0.5ºC

****Corresponding author:***
Email: abhi.sonje4u@gmail.com

2) Preparation of medium (Dilute Hydrochloric acid) [23]

Prepared by dissolving 80 ml conc.HCL Acid in 8000ml distilled wster.

Table-1 Formula for preparation of Propranolol tablets (160 mg)-

Ingredients	A1(mg)	A2(mg)	A3(mg)	A4(mg)
Propranolol HCL	160	160	160	160
Avicel pH102	100	100	96	96
Lactose monohydrate	100	100	100	100
PVP K90	16	16	16	16
Sodium starch glycolate	16	16	16	16
Aerosil	4	4	4	4
Magnessium stearate	4	-	8	-
Sodium stearyl fumarate	-	4	-	8

3) Standard Preaparation [23]

Transfer an accurately weighed quantity of about 32 mg of propranolol in 200ml dissolution medium.Then took 10 ml from that soln and dissolve in 50ml of dissolution medium.

4) Sample preparation [23]

Withdraw sample at each interval of 5, 10, 15, 20, 25 and 30 min.

Table-2 Formula for preparation of Carvedilol (3.125) tablets-

Ingredients	B1 (mg)	B2 (mg)	B3 (mg)	B4 (mg)
Carvedilol	3.125	3.125	3.125	3.125
Avicel pH102	32.5	32.5	32	32
Lactose monohydrate	32.5	32.5	32	32
PVP K90	5	5	5	5
Sodium starch glycolate	5	5	5	5
Aerosil	1	1	2	2
Magnessium stearate	1	-	2	-
Sodium stearyl fumarate	-	1	-	2

Carvedilol tablets [23]

1) Dissolution parameter [23]

Medium- 900ml, simulated gastric fluid with pepsin

Table-3 Formula for preparation of Atenolol (25 mg) tablets-

Ingredients	C1 (mg)	C2 (mg)	C3 (mg)	C4 (mg)
Atenolol	25	25	25	25
Avicel pH102	52	52	51	51
Lactose monohydrate	52	52	51	51
PVP K90	7.5	7.5	7.5	7.5
Sodium starch glycolate	7.5	7.5	7.5	7.5
Aerosil	5	5	5	5
Magnessium stearate	1.5	-	3	-
Sodium stearyl fumarate	-	1.5	-	3

Apparatus- USP-2 (Paddle)
RPM-50

Time- 5,10,15,20,25,30 min.
Temperature- 37°C±0.5ºC

Table-4 Formula for preparation of Hydrochlorothiazide (25 mg) tablets-

Ingredients	D1 (mg)	D2 (mg)	D3 (mg)	D4 (mg)
Hydrochlorothiazide	25	25	25	25
Avicel pH102	52	52	51	51
Lactose monohydrate	52	52	51	51
PVP K90	7.5	7.5	7.5	7.5
Sodium starch glycolate	7.5	7.5	7.5	7.5
Aerosil	5	5	5	5
Magnessium stearate	1.5	-	3	-
Sodium stearyl fumarate	-	1.5	-	3

make 6000 ml.

3) Standard Preaparation [23]

Transfer an accurately weighed quantity of about 70 mg of Carvedilol working standard to a 50ml volumetric flask.Then added about 25ml of Methanol and sonicated for dissolve.Made volume up to mark by Methanol.Dilute 5ml with 50ml and again 5ml with 100ml dissolution medium.

4) Sample preparation [23]

Withdraw sample at each interval of 5, 10, 15, 20, 25 and 30 min.

Atenolol tablets [23]

1) Dissolution parameter [23]

Medium-900 ml,0.1 N Acetate buffer pH 4.6
Apparatus- USP-2 (Paddle)
RPM-50
Time- 5,10,15,20,25,30 min.
Temperature- 37°C±0.5ºC

2) Preparation of medium [23]

Table 5 Results of In Process Parameters for Propranolol HCL.

Properties	Observation A1	Observation A2	Observation A3	Observation A4
Average weight	399 mg	398 mg	402 mg	399mg
Hardness	6-8 kp	6-8 kp	6-8 kp	6-8 kp
Friability	0.275 %	0.074%	0.258 %	0.089 %
Disintegration time	30-35 sec	15-20 sec	1-1.30 min	30-35 sec

2) Preparation of medium [23]

Prepared by dissolving 10gm of Sodium chloride and 19.2gm of purified pepsin in 18ml of conc.HCL acid and sufficient distilled water to

Prepared by dissolving 36.63 gm of Sodium acetate trihydrate in 1000 ml of distilled water.Then added 19 ml of Glacial acetic acid and dilute to 6000ml with distilled water.The resulting solution had pH 4.6 that adjusted by

Table 6 Results of In Process parameters for Carvedilol

Properties	Observation B1	Observation B2	Observation B3	Observation B4
Average weight	79 mg	78 mg	79.5 mg	78 mg
Hardness	4-5 kp	4-5 kp	4-5 kp	4-5 kp
Friability	0.319 %	0.164%	0.350 %	0.199 %
Disintegrat1ion time	20-25 sec	15-20 sec	1-1.30 min	30-35 sec

Table 7 Results of In Process parameters for Atenolol

Properties	Observation C1	Observation C2	Observation C3	Observation C4
Average weight	148 mg	149 mg	148.5 mg	151.5 mg
Hardness	4-5 kp	4-5 kp	4-5 kp	4-5 kp
Friability	0.215 %	0.059%	0.167 %	0.062 %
Disintegration time	15-18 sec	12-15 sec	20-25 sec	15-20 sec

Table 8 Results of In Process parameters for Hydrochlorothiazide

Properties	Observation C1	Observation C2	Observation C3	Observation C4
Average weight	149.5 mg	149 mg	152.5 mg	150.5 mg
Hardness	4-5 kp	4-5 kp	4-5 kp	4-5 kp
Friability	0.316 %	0.378%	0.254 %	0.236 %
Disintegration time	25-28 sec	20-25 sec	30-35 sec	25-30 sec

Glacial acetic acid.

3) Standard Preaparation [23]

Transfer an accurately weighed quantity of about 100 mg of Atenolol to 100 ml volumetric flask.Then added 50 ml of dissolution medium and sonicated for 5 min.Diluted 5 ml solution to 50 ml of dissolution medium.Further duluted 5 ml of solution to 50 ml of dissolution medium.Filtered the solution through 0.45um Millipore HVLP filter,collected filtrate by discarding first few ml of filtrate.

4) Sample preparation [23]

Withdraw sample at each interval of 5, 10, 15, 20, 25 and 30 min.

Hydrochlorothiazide tablets [23]

1) Dissolution parameter [23]

Medium-Dilute Hydrochloric acid (1 in 1000ml)
Apparatus- USP-1 (Basket)
RPM-100
Time- 5,10,15,20,25,30 min.
Temperature- 37°C±0.5ºC

2) Preparation of medium (Dilute Hydrochloric acid) [23]

Prepared by dissolving 80 ml conc.HCL Acid in 8000ml distilled wster.

3) Standard Preaparation [23]

Transfer an accurately weighed quantity of about 50 mg of Hydrochlorothiazide in 200ml dissolution medium.Then took 5 ml from that soln and dissolve in 50ml of dissolution medium.

4) Sample preparation [23]

Withdraw sample at each interval of 5, 10, 15, 20, 25 and 30 min.

RESULTS AND DISCUSSIONS

Dissolution Profile-

a) Propranolol Hcl-

Table 9: Dissolution Profile of Propranolol

Minutes	1% MGS	1% SSF	2% MGS	2% SSF
0	0	0	0	0
5	82.9	92.3	85.3	74.3
10	89.4	95.9	87.8	76.8
15	97.7	102.9	91.1	79.8
20	91.4	103.5	95.3	77
25	101	98.3	96.2	62.3
30	87.8	96.4	87.5	71.5

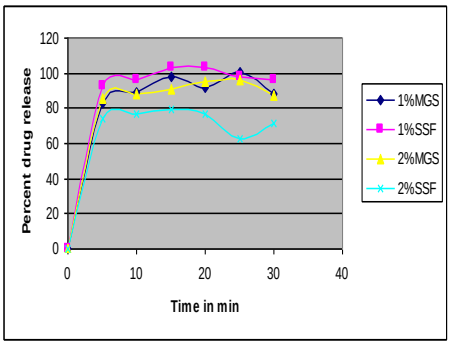

Fig.1 Dissolution Profile Of Propranolol Hcl Tablets

b) Carvedilol-

Table 10: Dissolution Profile of Carvedilol

Minutes	1% MGS	1% SSF	2% MGS	2% SSF
0	0	0	0	0
5	71.4	76.2	65.3	67.8
10	76.5	79.2	67.2	69.7
15	76.9	82.4	70.9	72.3
20	78.4	84.1	71.3	75.7
25	77.9	79.2	69.2	71.7
30	68.4	78.9	64.6	70.2

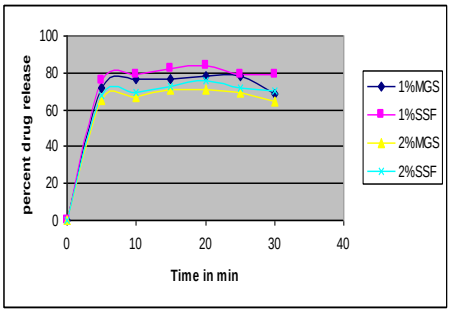

Fig.2 Dissolution Profile Of Carvedilol Tablets

c) Atenolol

Table 11: Dissolution Profile of Atenolol

Minutes	1% MGS	1% SSF	2% MGS	2% SSF
0	0	0	0	0
5	85.3	91.8	71.1	84.6
10	101.7	102.7	82.5	85.8
15	103.4	104.8	83.3	85.9
20	107.8	109.8	75.2	82.3
25	102.9	110.9	86.4	87.9
30	96.2	99.6	84.9	89.4

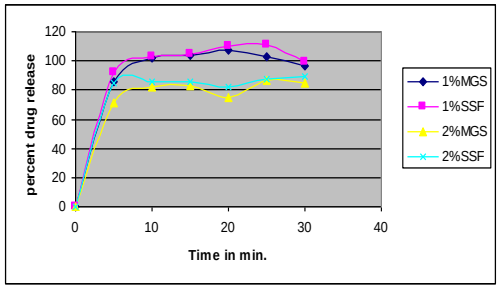

Fig.3 Dissolution Profile Of Atenolol Tablets

d) Hydrochlorothiazide-

Table 12: Dissolution Profile of Hydrochlorothiazide-

Minutes	1% MGS	1% SSF	2% MGS	2% SSF
0	0	0	0	0
5	73.4	80.3	60.8	63.8
10	78.9	80.6	69.3	68.7
15	79.7	82.4	70.1	70.6
20	80.2	86.9	71.8	69.7
25	80.9	79.2	64.5	80.5
30	77.9	84.1	71.3	74.3

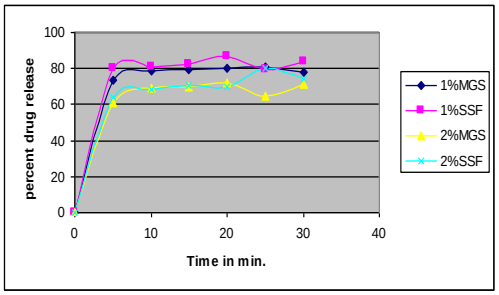

Fig.4 Dissolution Profile Of Hydrochlorthiazide Tablets.

SUMMERY AND CONCLUSION

The objective of this study was to study effect of lubricants on dissolution profile for antihypertensive drugs. As Propranolol HCL, Carvedilol, Atenolol and Hydrochlorothiazide used for proper management of diseases like hypertension.

From our study, it has been revealed that the retard of drug release increased as the concentration of lubricant increases. It was evident from the dissolution data that,Sodium stearyl fumarate releases more drug as compair to Magnessium stearate.

Magnessium stearate has the tendency to coat the individual particles to form hydrophobicity on the surface of individual particles.Due to which it reduces the drug release. Sodium stearyl fumarate showed good lubricant properties and remains discreet within the mixture without forming waxy or hydrophobicity on the surface of individual particles.

Evaluation of all *in-vitro* parameters was done and it was found that 1% Sodium stearyl fumarate shows satisfactory results as compair to 2% Sodium stearyl fumarate, 1% Magnessium stearate, 2% Magnessium stearate.

REFERENCES

1. Rubric E.M. Schwartz J.D. In: Oral Solid Dosage Form, In: Remington, The Science and Practice of Pharmacy, 20th edition, 1, 2001, 859-871.

2. Banker G.S.,Anderson N.R.,In: The Theory and Practice of Industrial Pharmacy,Lachman L.,Liberman H.A.,Kanig J.L., 3rd edition, Vanghese publishing house, 293-345.

3. Carter J.C., (2001).Carter Pharmaceutical Councelling, Role of Lubricants 2001-2006.

4. Tripathi K.D., Essentials of Medical Pharmacology, Jaypee brothers, Medical publisher, 6th edition,539-554,136-144.

5. Bogda M.J.,Tablet Compression Machine Theory, Design and Process Trouble Shooting In-Encyclopedia of Pharmaceutical technology,Vol-2,Marcel Dekker Inc Newyork,2002,2669-2674.

6. Loyd V. Allen,Jr, Nicholas G.Popvich,Howard C. Ansel,In: Ansels Pharmaceutical dosage forms and drug delivery system, 8th edition.

7. Tousey MD,"Pharmaceutical Technology,Tabletting and Granulation"(http//www.pharmatech.com)

8. Joshi V., Excipients Choice in Solid Oral Dosage Form, Drug Delivery Technology,Vol-2, 2002,36-40.

9. Vladi O.Consiglieny,Tiago Martinello,Telma marrie kaneco,Maria Elena Santos,In: Optimisation of Poorly Compatible Drug Tablets, Manufactured by Direct Compression Using the Mixture Experimental Design, Int. Journal of Pharmaceutics,Vol-322,2006,87-95.

10. J.Martin Bultmann, Multiple Compaction of Mycrocrystalline Cellulose in A Roller Compactor, European Journal of Pharmaceutics and Biopharmaceutics, VOL-54,2002,59-64.

11. Albert Mihranym, Moisture sorption by Cellulose powders of varing Crystalanity, 2004.

12. Fitzpatrick Shaun, Mecable James, In: Effect of Moisture on Polyvenyl Pyrrolidine, Int.Journal of Pharmaceutics, 2002, Vol 246.

13. Bolhuis G.K.,In:Effect of Magnessium Stearate on Disintegration of tablets, Department of Pharmaceutical Technology and Biopharmaceutics, Vol 179.

14. Hussain, Shah V.P. In: The Biopharmaceutical Classification System, Highlights of the FDAs draft Guidence, Office of pharmaceutical sciences, CDER,FDA,Rockvile MD.

15. Biopharmaceutical Classification System, http://www.fda.gov/cder.

16. http://www.drugs.com.

17. http:www.rxlist.com/voltaren_drug.htm.

18. http://en.wikipedia.org

19. Rowe, R. C., Sheskey, P. J., Weller, P. J., (2003). Handbook of Pharmaceutical Excipients (4th Ed.). The Pharmaceutical Press, Great Britain, 108-608.

20. Banker G. S. Rhodes, C. T. (2002). Modern Pharmaceutics, Dekker, New York, 125-135.

21. ICH Guidelines Q1A (R2)"Guidence for Industry, Stability Testing of New Drug Substance and products"(http//www.ich.org).

22. M.E.Aulton, Pharmaceutics, The science of dosage form design,Churchill Livingstone,2nd edition,2002.

23. The United State Pharmacopoeia / The National Formulary (2007). The United State Pharmacopoeia Convention, Rockville, MD, Volume-II, USP30/NF25 edition.

24. Costa, P., Sousa Lobo, J. M., (2001). Modelling and comparison of dissolution profiles. European Journal Pharmaceutical Science, 13, 123-133.

25. Guidence for industry "Dissolution Testins of Immediate Release Solid Oral Dosage Forms"US department of Health and Human Services FDA, CDER, August 1997 BPI.