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Research article ***Pharmaceutical Sciences***

Influence of dissolution media and pH on the dissolution characteristics of diclofenac sodium pure drug

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ABSTRACT

The present study was performed to illustrate the effect of different dissolution media and PH on dissolution profile of diclofenac sodium sustained release of granules. Diclofenac sodium has analgesic antipyretic and anti-inflammatory activities. It is a potent relatively non selective Cyclooxygenase inhibitor. It is absorbed rapidly and completely after oral administration; peak concentration in plasma reached with-in 2-3 hours. The drug extensively binds to plasma protein (99%) and its half-life in plasmais1-2hours. Diclofenac sodium extended release are prescribed for long symptomatic treatment of Rheumatoid arthritis, Osteo-arthritis. The PH buffer selection bases on exposer of drug from stomach to intestine and ensure the impact of P^H changes on dissolution and release of drug substance for absorption. Dissolution is used to show the release of drug from the tablet is close to 100%. The dissolution behavior of drug in a particular media permits *the selection of right dissolution medium which gives in-vivo and in-vitro correlation.* Based on the ingredients present in dissolution, it is possible to formulate a dosage form with those ingredients to improve dissolution.

Keywords: Diclofenac sodium, dissolution studies, pH

INTRODUCTION

The dissolution of a substance refers to its ability to dissolve in a solvent or dissolution medium. The choice of dissolution media and the pH of the medium can significantly influence the dissolution behavior of a substance. Here's how dissolution media and pH can affect the dissolution process:

Dissolution Media

The choice of dissolution media is critical because it should mimic the physiological conditions under which the substance is intended to be administered. Different dissolution media are used to simulate various biological environments, such as gastric fluid, intestinal fluid, or other specific physiological conditions.

The composition of the dissolution media, including salts, surfactants, and enzymes, can impact the solubility and dissolution rate of the substance. For example, the presence of bile salts in intestinal fluid can enhance the dissolution of lipid-soluble substances. Similarly, the presence of enzymes, such as pancreatin, can facilitate the dissolution of certain pharmaceuticals.

Additionally, the volume and agitation rate of the dissolution media can affect the dissolution process. Higher volumes and increased agitation can improve the sink conditions, maintaining a constant concentration gradient and promoting faster dissolution.

pH

The pH of the dissolution media plays a crucial role in determining the ionization and solubility characteristics of substances. The pH affects the degree of ionization of acidic or basic substances, which can impact their solubility and dissolution rate.

Acidic substances tend to dissolve more readily in acidic media, while basic substances often dissolve better in basic media. The pH can influence the ionization of functional

groups present in the substance, thereby affecting its solubility. For instance, a weakly acidic drug may be more soluble in an acidic medium because it remains unionized, whereas in a basic medium, it may ionize and become less soluble.

In the case of drugs, the pH of the dissolution media can be particularly important. It can affect the drug's absorption and bioavailability, as the solubility of the drug in the gastrointestinal tract can impact its dissolution and subsequent absorption into the bloodstream.

The choice of dissolution media and pH can significantly influence the dissolution behavior of a substance. Proper selection of dissolution media that closely represents the physiological conditions and controlling the pH within a relevant range are essential to accurately simulate the dissolution process and predict the substance's behavior in biological systems.

Diclofenac sodium

Diclofenac sodium, a phenyl acetic acid derivative, is anon-steroidal, anti- inflammatory, the Molecular formula of Diclofenac sodium is C14H10O2CL2N.Na and chemical name,2-[(2,6dichlorophenyl)-amino] phenyl acetate. It is freely soluble in methanol, soluble in ethanol (95%), sparingly soluble in water and glacial acetic acid, practically insoluble in ether, chloroform and toluene. Diclofenac has analgesic, antipyretic and anti-inflammatory activities.

Dissolution

Dissolution is a process in which a solid substance solubilizes in a given solvent i.e mass transfer from the solid surface to the liquid phase.

MATERIALS & METHODS

The list of materials and instruments used in the experiment were of analytical grade/ laboratory grade.

S.NO	Materials	Grade	Supplier
1	Diclofenac sodium	Pharma	Vikas College of Pharmaceutical Science
2	Potassium di-hydrogen phosphate	Pharma	Vikas College Of Pharmaceutical Science
3	Sodium hydroxide	Pharma	Vikas College Of Pharmaceutical Science
4	Starch	Pharma	Vikas College Of Pharmaceutical Science
5	Talc powder	Pharma	Vikas College Of Pharmaceutical Science
6	Starch paste	Pharma	Vikas College Of Pharmaceutical Science
7	Distilled water	Pharma	Vikas College Of Pharmaceutical Science

SI.NO	Instruments	Manufacture/Suppliers
1	UV Visible spectrophotometer	ELICO.SL-164
2	Magnetic stirrer	Paramount Scientifics
3	Dissolution apparatus	LABINDIA
4	Digital Ph meter	Secor India
5	Sonicator	Q sonica
6	Electronic precision balance	Contech.CA 223
7	Hot air oven	Teknik

METHODOLOGY

Preparation of diclofenac sodium granules

Weigh accurately 10gms of diclofenac sodium and taken into the motor & pestle and weigh the starch and talc then they are mixed together with diclofenac sodium in motor pestle. Then the starch gel is prepared for wetting the mixture of drug.

Starch Gel Preparation

(Weigh accurately 10gms of starch and mix in sufficient amount of water then place a water bath and heat the 25-30 ml of water in beaker and slowly add the starch mixture and stir thoroughly until it make gel form, allow it to cool at room temperature.)

- Then add the starch gel quantity sufficient (qs) to the mixture until it form sweet cohesive mass.
- The mass was screened in a sieve mesh (size:20) until it forms granules.
- The granules are allow to dry for 15-20 minutes in Hot air oven at 60^{o}C.
- The moisture content is determined usually by IR moisture balance.

  1 gram in each.
- Then the granules are weighed and recorded.
- The granules are taken into masculine clothe for

Formulation design

S.No	INGREDIENTS	QUANTITYREQUIRED
01.	Potassium dihydrogen phosphate(KH_2PO_4)	250ml
02.	Sodium hydroxide (NaOH)	195.5ml(7.4)/173.4ml(7.2)
03.	Diclofenac sodium pure drug (granules)	100mg
04.	Starch	0.5gms
05.	Starch paste	10gms
06.	Talc powder	0.1gm
07.	Distilled water	q.s

Dissolution method

- The prepared granules are dissolute in dissolution apparatus, (dissolution apparatus company name: LABINDIA and Model of the apparatus: DISSO 2000).
- The water bath is filled with water and the temperature prob is placed in water bath it is maintained upto37^{o}c.
- Then take the granules in masculine cloth and tie it tightly to the paddles Operate it with100RPM or (25 RPM per 4 mins).
- Every10 mins take2 ml of solution from distilled water, ph 7.2 and 7.4 with the help of syringe.
  We need to replace 2ml water to water pH 7.2 to7.2and7.4to7.4respectively to maintain sink condition
- As this process need to be continued until the granules get dissolved completely.
- By taking 2ml of water pH7.2and pH7.4 for every 10 minutes make up it up to10ml of water pH7.2 and 7.4 respectively.
- The USP dissolution apparatus consists of 8 baskets.
- In 8 baskets, 6 baskets are filled with distilled water and 2 baskets are filled with p^{h} 7.4, 7.2.
- Each basket consists of 900 ml of water and p^{H} buffer 7.2 and7.4respectively.
- The solutions are poured into cuvettes and measure the absorbance by using uv visible spectrophotometer

Evolution of granules

1. Particle size and shape determination
2. Surface area
3. Density

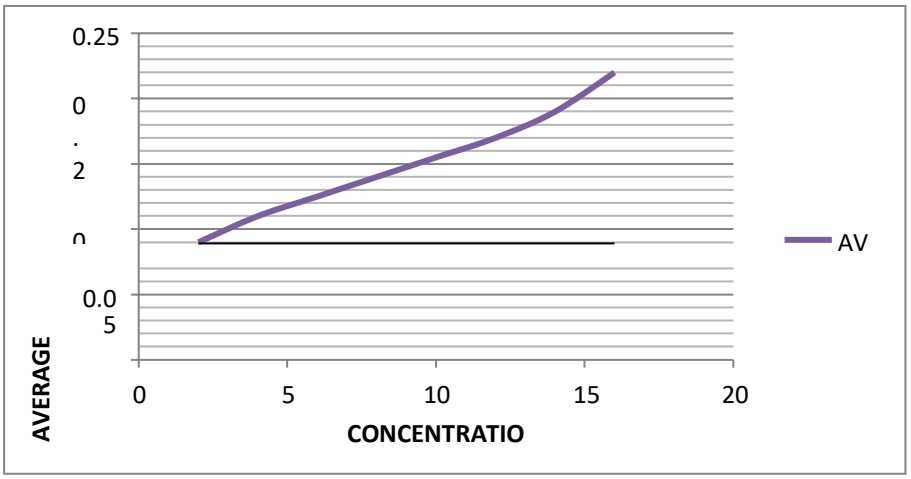
Bulk density True density Granular density

4. Granule strength and friability
5. Flow properties Angle of repose

Percentage compressibility index Hausner's ratio

6. Moisture content
7. Percentage fines

RESULTS AND DISCUSSION

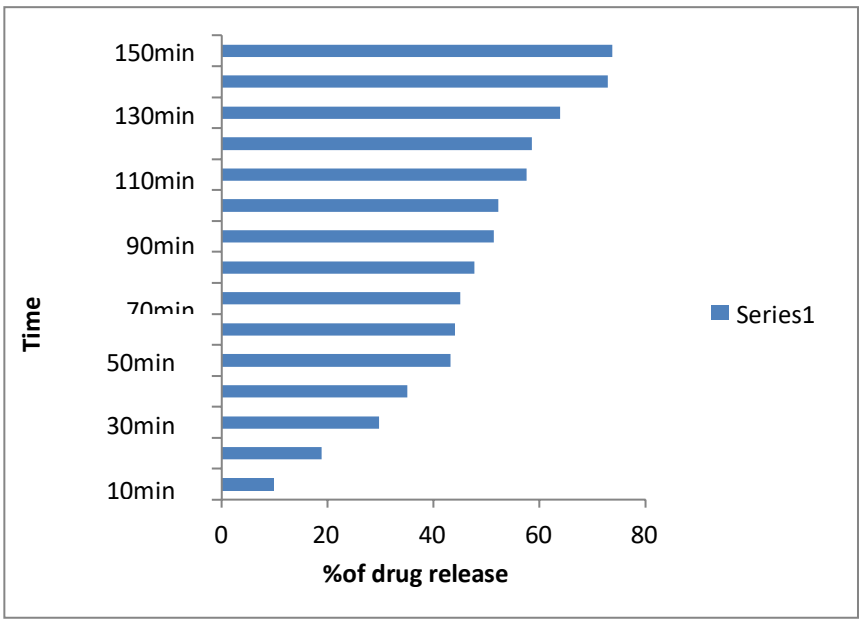


The spectrum of UV was analyzed by UV/ Vissible spectroscopy and λ^{max} found to be 276nm at pH7.4 with Calibration curve of Diclofenac sodium-@276nm.

CONC(mg/ml)	Abs1	Abs2	Abs3	Avg
2	0.0376	0.0398	0.0385	0.09
4	0.0527	0.0501	0.0533	0.11
6	0.0578	0.0513	0.0512	0.125
8	0.0598	0.0612	0.0602	0.14
10	0.0622	0.0705	0.0712	0.155
12	0.0745	0.0716	0.0725	0.17
14	0.0888	0.0799	0.0824	0.19
16	0.0911	0.0998	0.0988	0.22

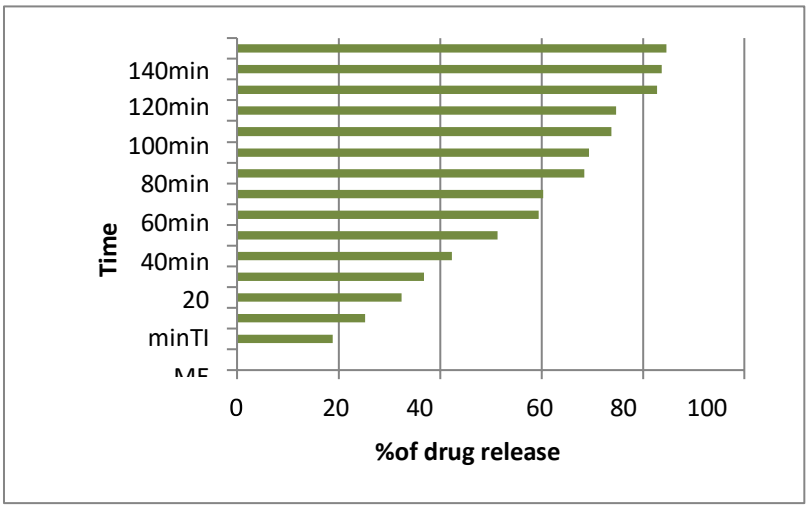
P^H7.2

Time	%Amount of drug release
10mins	9.9
20mins	18.9
30mins	29.7
40mins	35.1
50mins	43.2
60mins	44.1
70mins	45
80mins	47.7
90mins	51.3
100mins	52.2
110mins	57.6
120mins	58.5
130mins	63.9
140mins	72.9
150mins	73.8

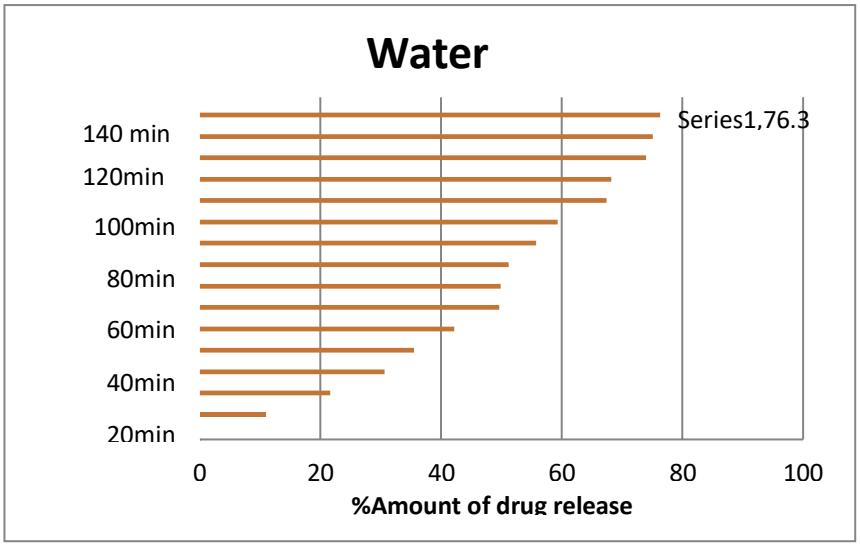


P^H 7.4

Time	%Amount of drug release
10mins	18.9
20mins	25.2
30mins	32.4
40mins	36.9
50mins	42.3
60mins	51.3
70mins	59.4
80mins	60.3
90mins	68.4
100mins	69.3
110mins	73.8
120mins	74.7
130mins	82.8
140mins	83.7
150mins	84.6

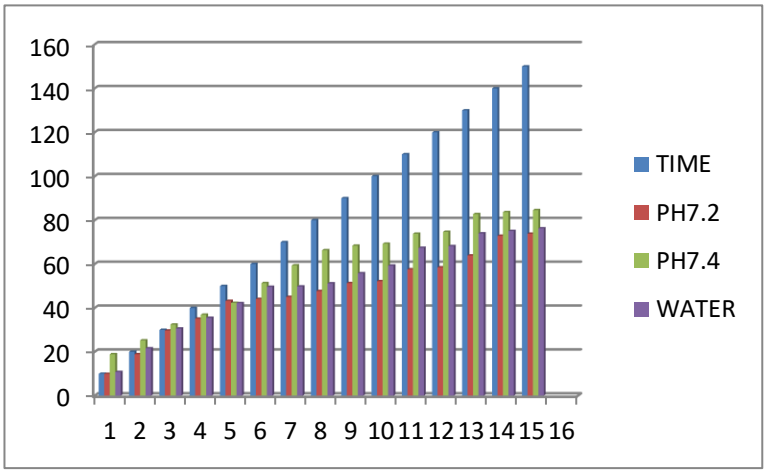


TIME	% AMOUNT OF DRUG RELEASE
10min	10.8
20min	21.6
30min	30.6
40min	35.5
50min	42.2
60min	49.6
70min	49.8
80min	51.2
90min	55.8
100 min	59.3
110 min	67.4
120 min	68.2
130 min	74.0
140 min	75.1
150 min	76.3



COMPARISONTABLE

TIME	P^H7.2	P^H7.4	WATER
10min	9.9	18.9	10.8
20min	18.9	25.2	21.6
30min	29.7	32.4	30.6
40min	35.1	36.9	35.5
50min	43.2	42.3	42.2
60min	44.1	51.3	49.6
70min	45	59.4	49.8
80min	47.7	60.3	51.2
90min	51.3	68.4	55.8
100min	52.2	69.3	59.3
110min	57.6	73.8	67.4
120min	58.5	74.7	68.2
130min	63.9	82.8	74.0
140min	72.9	83.7	75.1
150min	73.8	84.6	76.3



CONCLUSION

Present study was effect of dissolution media and P^H on drug release behavior of diclofenac sodium pure drug.

For this study different dissolution mediums are used like distilled water, phosphate buffer and also different P^H like 7.2 & 7.4. PBS

The dissolution behavior of drug in a particular media permits the selection of right dissolution medium which gives in-vivo and in-vitro correlation. Based on the ingredients present in dissolution, it is possible to formulate a dosage form with those ingredients to improve dissolution.

Dissolution is the important parameter for selecting the suitable dosage forms for therapeutic success of drugs.

When the dissolution media changes percentage of drug release changes, interestingly when pH of the medium changes there is a change in drug release observed.

When the pH of the phosphate buffer changes from 7.2 to 7.4 percentage of drug release increases from 73.8 to 84.6 in 150 min.

When dissolution medium changes from distilled water to phosphate buffer there is slight change in percentage of drug release was observed.

Based on above results that can be concluded as dissolution media and pH of the dissolution media shows the impact on drug release behavior of drugs. Based on above conclusion the dissolution behavior of drug in a particular media permits the selection of right dissolution medium which gives *in-vivo* and *in-vitro* correlation.

REFERENCES

1. Dressman JB, Amidon GL, Reppas C, Shah VP. Dissolution testing as a prognostic tool for oral drug absorption: immediate release dosage forms. Pharm Res.1998;15(1):11-22. doi: 10.1023/a:1011984216775, PMID 9487541.
2. Galia E, Nicolaides E, Hörter D, Löbenberg R, Reppas C, Dressman JB. Evaluation of various dissolution media for pre dicting in vivo performance of class I and II drugs. Pharm Res.1998;15(5):698-705. doi: 10.1023/a:1011910801212, PMID 9619777.
3. Sheng JJ, Kasim NA, Chandrasekharan R, Amidon GL. Solubilization and dissolution of insoluble weak acid, ketoprofen: effects of pH combined with surfactant. Eur J Pharm Sci.2006;29(3-4):306-14. doi: 10.1016/j.ejps.2006.06.006, PMID 16982177.
4. Kostewicz ES, Wunderlich M, Brauns U, Becker R, Bock T, Dressman JB. Predicting the precipitation of poorly soluble weak bases upon entry in the small intestine. J Pharm Pharmacol.2004;56(1):43-51. doi: 10.1211/0022357022511, PMID 14980000.
5. Carlert S, Pålsson A, Hanisch G, von Corswant C, Nilsson C, Lindfors L, et al. Predicting intestinal precipitation—a case ex ample for a basic BCSclass II drug. Pharm Res.2010;27(10):2119-30. doi: 10.1007/s11095-010-0213-8, PMID 20717839.
6. Tsume Y, Mudie DM, Langguth P, Amidon GE, Amidon GL. The Biopharmaceutics Classification System: subclasses for in vivo predictive dissolution (IPD) methodology and IVIVC. Eur J Pharm Sci.2014;57:152-63. doi: 10.1016/j.ejps.2014.01.009, PMID 24486482.
7. Kukec S, Dreu R, Vrbanec T, Srčič S, Vrečer F. Characterization of agglomerated carvedilol by hot- melt processes in a fluid bed and high shear granulator. Int J Pharm.2012;430(1-2):74-85. doi: 10.1016/j.ijpharm.2012.03.041, PMID 22486965.
8. MahmoudEA,BendasER,MohamedMI. Preparation and eval uation of self-nanoemulsifying tablets of carvedilol. AAPS PharmSciTech. 2009;10(1):183-92. doi: 10.1208/s12249-009-9192-7, PMID 19238556.
9. Stillhart C, Dürr D, Kuentz M. Toward an improved under standing of the precipitation behavior of weakly basic drugs from oral lipid-based formulations. J Pharm Sci.2014;103(4):1194-203. doi: 10.1002/jps.23892, PMID 24515977.
10. Loftsson T, Vogensen SB, Desbos C, Jansook P. Carvedilol: sol ubilization and cyclodextrin complexation: a technical note. AAPS PharmSciTech. 2008;9(2):425-30. doi: 10.1208/s12249-008-9055-7, PMID 18431667.