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QUALITY ASSESSMENT OF INDOMETHACIN CAPSULES MARKETED BY BANGLADESHI PHARMACEUTICAL INDUSTRIES

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Abstract: In Bangladesh about nineteen different Indomethacin marketed preparations (including capsule and suppository) are available. Of them nine brands are Indomethacin capsule dosage forms, potency of which was assayed by UV spectrophotometry and dissolution study was carried out according to the USP pharmacopoeial method to evaluate their quality. The result showed that eight brands of capsules (89%) met the USP specification of potency and the remaining one brand was less potent. All brands were tested for dissolution rate and two brands (23%) failed to meet the specification for dissolution rate. Additional in-vivo bioavailability studies are of utmost importance to draw more conclusive finding regarding quality status of the Indomethacin preparations.

Key words: Capsule, Indomethacin, dissolution test, potency, pharmaceuticals, Bangladesh

Introduction

Indomethacin is a widely used antipyretic and anti-inflammatory drug. This drug relieves fever by affecting hypothalamus, and blocks the action of cyclooxygenase, thus act as an anti-inflammatory agent (Hardman *et al.*, 1996).

Studies conducted previously on the release pattern of Indomethacin, but most of these were to examine the *in-vivo* bioavailability pattern. A series of 24-hour repeated experiments was conducted to evaluate the changes in release pattern, bioavailability and effects of Indomethacin in healthy subjects (Clench *et al*., 1981). Pharmacokinetic study of prolonged release form of Indomethacin was also conducted (Guisson *et al.,* 1983).

The rate of drug dissolution may be directly proportional to the efficacy of the product. In *in-vitro* testing procedures, dissolution test is the only test that can more or less indirectly correlate the *in-vivo* bioavailability (Tripathy, 2000). Again, dissolution is the prime factor for proper absorption of the drug particles and ultimately bioavailability of the drug (Miyagawa *et al.*, 1996). Therefore, the present study was undertaken to evaluate the quality of reputed Indomethacin capsule brands available in local market in terms of dissolution profile and drug content.

Materials and Methods

Nine brands of Indomethacin capsules were purchased from the different wholesale and retail medicine shops of Khulna city. The samples were collected in such a way that some samples were immediately after manufacturing, some were just before their expiry dates and others were intermediate of two kinds to know about the stability status of the drug products during their shelf-life. The samples were properly checked for

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their physical appearance, name of manufacturer, batch number, manufacturing date, expiry date, manufacturing license number, D.A.R. number and maximum retail price at the time of purchase. The samples were then coded with ethics (IC 01to IC 09) for analysis. The labels of all the brands claimed to contain 25 mg of Indomethacin per capsule.

The USP reference standard of Indomethacin powder was collected from Aristopharma Ltd., Bangladesh. The purity of the reference standard was 99.54%. Disodium hydrogen phosphate, monobasic potassium phosphate and sodium hydroxide have been purchased from E. MERK (India) Ltd. Methyl chloride was collected from Loba chemie pvt. Ltd., India and citric acid from BDH Chemicals Ltd., England.

In-vitro drug release studies were conducted using type-I USP dissolution apparatus at 37±0.5 °C. Apparatus was operated at 100 rpm in pH 7.2 phosphate buffer (Anon, 2000a). Then 10 ml of the fluid was withdrawn after 20 minutes. The percentage of Indomethacin dissolved was determined from UV absorbance at the wavelength of 318 nm of filtered portion of the solution under test, suitably diluted with distilled water in comparison to a standard Indomethacin solution having known concentration of USP Indomethacin RS in the same medium.

A UV spectrophotometer (Camspec, UK) was used to determine the amount of Indomethacin present in the sample at 318 nm by using methylene chloride as the blank and compared with the standard sample of the drug. The quantity, in mg, in the portion of the capsules was determined by the formula:

% Potency = Au/As X 100.

Where, Au = Absorbance of assay preparation; and, As = Absorbance of standard preparation.

Results

Dissolution study: The dissolution study of Indomethacin capsules was carried out in a buffer media (pH 7.2 phosphate buffer). All the brands were found to satisfy USP specification of dissolution rate except IC 05 and IC 08. Dissolution rate of different brands of Indomethacin capsules is demonstrated by Table 1.

Table1. Dissolution rate of various brands of Indomethacin capsules (IC-01 to IC-09).

Sample code	% drug released after 20 minutes	USP specification
IC 01	96.75	Satisfied
IC 02	94.32	Satisfied
IC 03	86.32	Satisfied
IC 04	84.62	Satisfied
IC 05	76.98	Not satisfied
IC 06	83.56	Satisfied
IC 07	85.65	Satisfied
IC 08	76.45	Not satisfied
IC 09	84.68	Satisfied

USP specification: Not less than 80% of the labeled amount of indomethacin is dissolved for 20 minutes.

Potency determination: The potency of nine brands of Indomethacin capsules was determined as per procedure and the obtained results are illustrated in the Fig. 1.

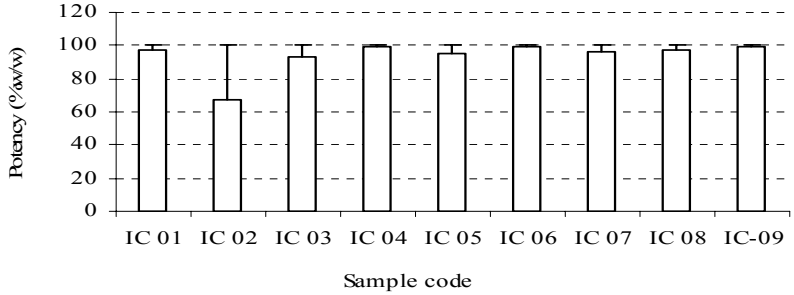

Fig.1. Potency of different Indomethacin capsule brands with percent deviation (IC 01 to IC 09).

Table 2 also does illustrate the estimated amount of Indomethacin per capsule in mg. with percent deviation and based on that deviation compliance or non-compliance with BP specification. From the obtained result, it was evident that all the brands met the BP specification (Anon, 2000b) of potency except IC 02.

Table 2. Potency status of the samples of indomethacin capsules (IC 01 to IC 09).

Code	Declared amount per capsule (mg)	Indomethacin per capsule (mg)	Percent deviation	Observation
IC 01	25	96.93	-3.07	Compliance
IC 02	25	67.74	-32.6	Non-compliance
IC 03	25	93.54	-6.48	Compliance
IC 04	25	99.54	-0.46	Compliance
IC 05	25	94.84	-5.15	Compliance
IC 06	25	99.01	-0.99	Compliance
IC 07	25	95.89	-4.11	Compliance
IC 08	25	97.71	-2.29	Compliance
IC 09	25	99.01	-0.99	Compliance

BP specification: (90-110) % w/w

Discussion

Indomethacin capsule brands, IC 05 and IC 08, may release comparatively low amount of drug in solution. Such a poor dissolution property of these two commercial brands may be due to improper selection of formulation ingredients as well as incorrect manufacturing procedure. Ultimately, such an event may affect the bioavailability of these particular brands. Relatively slow rate of dissolution in comparison to other brands may also affect the desired biological activity of these two reputed brands, as it is possible to correlate dissolution rate with the biological activity of active ingredient (Miyagawa *et al*., 1996).

The brand IC 02 was proved severely less potent and therefore definitely a substandard one. The low potency of IC 02 may be due to the degradation of active ingredient at the time of manufacturing or at any other stage of shelf life. There is another possibility of being less potent due to addition of less amount of active ingredient at the time of manufacturing.

Conclusion

The work covered only Indomethacin capsule dosage forms available in Bangladesh. These are insufficient to demonstrate the overall quality status of Indomethacin products of local market. Besides, additional in-vivo bioavailability studies are of utmost importance to draw conclusion regarding quality status of the samples.

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