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Comparative Evaluation of the Biopharmaceutical and Chemical Equivalence of the Some Commercial Brands of Paracetamol Tablets

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***Abstract*—**Acetaminophen (Paracetamol) tablets are popular OTC products among patients as analgesics and antipyretics. Paracetamol is marketed by a lot of suppliers around the world. The aim of the present investigation was to compare between many types of paracetamol tablets obtained from different suppliers (six brands produced by different pharmaceutical companies in middle east countries, and Panadol® manufactured in Ireland), by different quality control tests according to USP pharmacopeia.Using Non official tests-hardness and friability; official tests- disintegration, dissolution, and drug content. Additionally, evaluate the influence of temperatures 4˚C, 25˚C and 40˚C at 75% relative humidity on the stability of the same brands in their original packaging has been conducted for two months. The results revealed that all paracetamol tablet brands complied with the official USP specifications. In conclusion, paracetamol tablets preferred to be stored at 25˚C. All the tested brands being biopharmaceutically and chemically equivalent.

***Keywords*—**Non official tests-hardness and friability; official tests –disintegration, dissolution, and drug content.

I. Introduction

PARACETAMOL is a non-steroidal anti-inflammatory drug (NSAID) and is prescribed most frequently. It is also commonly used as analgesic and antipyretic agent in the relief of fever, headaches, other minor aches and pains [1]. Chemically, it is 4-hydroxy acetanilide (acetaminophen) [2]. Generally, paracetamol is safe for human use at recommended doses. But, overdoses of paracetamol can cause potentially fatal liver damage and in rare individuals, a normal dose can do the same. In addition, safety and efficacy of a pharmaceutical dosage form can be guaranteed when its quality is reliable. Generally, the efficacy of pharmaceutical dosage forms depends on their formulation properties, and manufacturing methods, hence it is likely that the quality of dosage form may vary [3]. Dissolution test is one of the in vitro tests usually employed to assess the quality of oral pharmaceutical solid dosage forms such as tablets and capsules [4]. In vitro dissolution tests can be used to guide formulation developments, identify critical manufacturing variables, monitor formulation quality from batch to batch and also serve as a surrogate for bioavailability and bioequivalence [5]**.**

II. Objective

Evaluation of biopharmaceutical and chemical equivalency of the tested brands.

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Evaluate the effects of different formulations of the selected brands of paracetamol tablets and the manufacturing processes on the quality control parameters according to USP specifications. Comparison between the dissolution profile of products under test to identify the critical manufacturing variables and to predict the in vivo performances and also to serve as a surrogate for the biopharmaceutical and chemical equivalence. Comparison of the stability of the tested brands by storage at temperatures 4˚C, 25˚C and 40˚C at 75% relative humidity over a period of two months .

III. Materials and Methods

Different brands of Acetaminophen were obtained from the market (Fevadol® 500 mg**,** Panadrex® 500 mg, Paracetamol® 500 mg, Pyral® 500 mg , Revanin® 500 mg tablets**,** Panadol® 500 mg tablets and Panda® 500 mg caplets). Acetaminophen pure powder (laboratory chemical reagent, market Harborough). The evaluation were done according to USP standard: Non official tests-hardness and friability ; official test –disintegration , dissolution and drug content, Additionally , evaluate the influence of temperatures 4˚C, 25˚C and 40˚C at 75% relative humidity on the stability of these brands in their original packaging over a period of two months . Then the tablets were evaluated for their physical properties and their release kinetics. Statistical data analysis and study of the release kinetic were achieved by fitting the data to the release models; Zero order, first order , Hixon – crowel, Higochi and Koresmeyer-Peppas.The order and the mechanism of drug release were investigated.

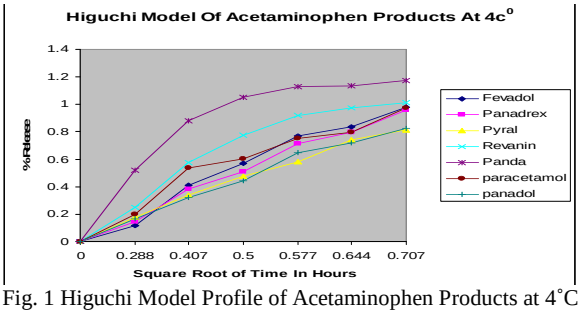

Fig. 1 Higuchi Model Profile of Acetaminophen Products at 4˚C

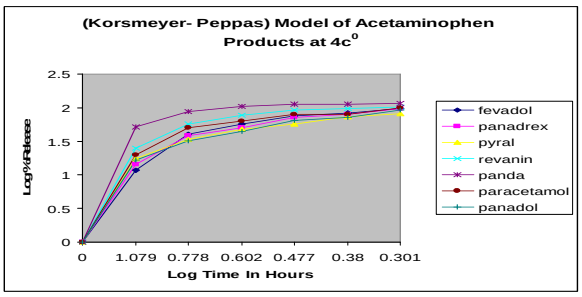

Fig. 2 Korsmeyer –Peppas Profile of Acetaminophen Products at 4 ˚C

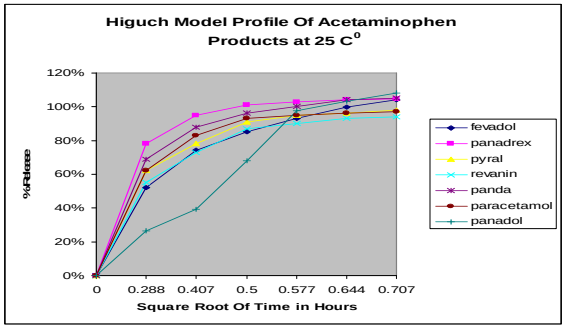

Fig. 3 Higuchi Model Profile of Acetaminophen Products at 25ºC

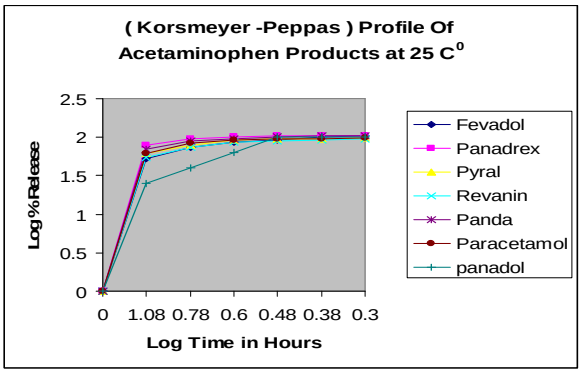

Fig. 4 Korsmeyer –Peppas Profile of Acetaminophen Products at 25ºC

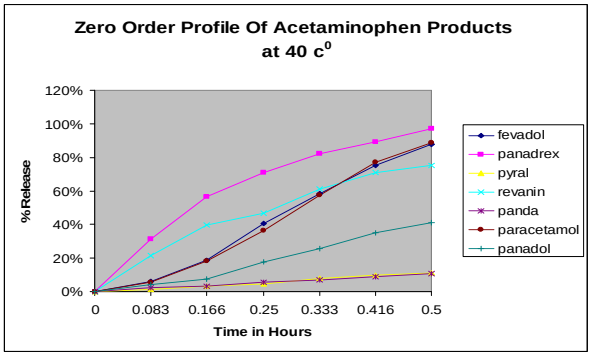

Fig. 5 Zero Order Profile of Acetaminophen Products at 40ºC

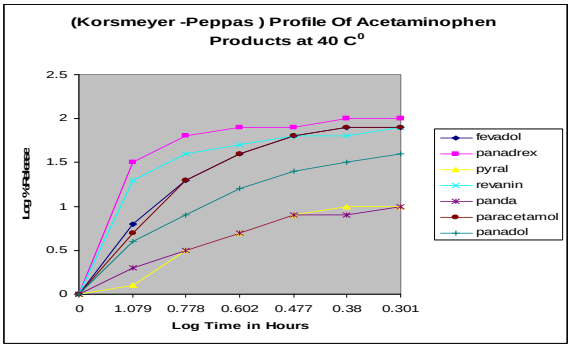

Fig. 6 Korsmeyer –Peppas Profile of Acetaminophen Products at 40ºC

IV. Results and Discussion

The results of the present study revealed that all the Arabic commercial brands are meeting the USP requirements of the quality control tests .No weight variation was estimated for all brands. The friability test was accepted for all brands except the , Revanin® tablets were more fragile (1.9%), which may be due to the nature of the binders and additives used in the manufacturing procedures. All the tablets were disintegrated within 30 minutes. The assay results (drug content) ascertain the presence and the quantity of paracetamol in all these products were (95-105%) except Pyral® and Paracetamol® did not comply with the drug content test. The *in vitro* dissolution profiles were found to be varying for each tablet, but within the prescribed limit [6].

Since the analgesic, antipyretic medications like Acetaminophen, used by patients to relief pain within short time (5-15) minutes. Therefore, it is preferred the fast drug release in order to relief the pain and decrease the fever within short time. The Panadrex® 500 mg tablets are preferred than the other acetaminophen products for faster release of pain and fever.

The study of the release kinetics showed that the higher values of correlation coefficient R2 obtained from release profile of the Acetaminophen products were with Higuchi Model at 4ºC (average R2= 0.9816) and 25ºC(average R2= 0.947). But, the release was obeyed the zero order at 40ºC. The mechanism of reaction was confirmed with Korsmeyer-peppas model. The model indicated that the drug release follow the fickian diffusion in case of tablets stored at 25ºC the average value was less than 0.45 (average n value =0.260) for the tested products. According to the value of n value in which the average was above 0.89 (average n value =1.87 and 0.952) for the tested products which indicate case -2 relaxation or super case transport-2 at 4ºC and 40ºC respectively.

At different temperature, the drug release was more than 80% after 30 minutes for all brands. In contrast, the release was lower than 80 % at 40˚C for Pyral® , Revanin® and Panadol® tablets, more over the drug release in case of Panda® caplets did not comply with official tests at 4˚C, and 40˚C .Additionally , after storage at 40ºC the disintegration time of these brands were not exceed 30 minutes , but for the Paracetamol® tablets stored at 40˚C , the disintegration was more than 30 minutes.

V. Conclusion

In the present study, the six Arabic commercial products of paracetamol were physically and chemically equivalent to each others with some exceptions.

There was no weight variation between the tablets of each batch. All tablets have a good mechanical strength and all products are complying with the friability test. .All formulations were disintegrated within 15-30 minutes .The fast disintegrated drug will improve the absorption of the drug.

Furthermore, the antipyretic and analgesic effects will be very fast to relief the pain.

All products are considered within the accepted range of drug content tests. The differences in the range is due to different additives and manufacturing mechanism used in different factories.

The release of active ingredient Acetaminophen from tablets was immediate release more than 80% was released within 30 min.

All brands were also physically and chemically equal after storage for 2 months at different temperatures. The kinetic of drug release revealed that the order of reaction obeys the Higuchi Model (which suggests the drug release by diffusion) at 25ºC. At 4ºC the reaction obeys also the Higuchi Model but the release mechanism was case -2 relaxation or super case transport-2 which was also the mechanism after storage at 40ºC but in this case the order of the reaction was zero order.

In conclusion, all the brands tested in this study were physically and chemically equivalent and it is preferred to store them at 25ºC.

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