FORMULATION, EVALUATION AND PHARMACOKINETICS OF FLURBIPROFEN FAST DISSOLVING TABLETS

A Case Study by Opeyemi Orhekafore BEDU, Nigeria
(B.LMS in Histopathology, M.Sc Clinical Research Student of Texila American University)
Email: orhekabedu@yahoo.com

Fast dissolving tablets disintegrate and dissolve rapidly in the saliva without the need for water. This tablet format is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Flurbiprofen is an anti-inflammatory and analgesic drug used in the treatment of chronic rheumatoid diseases which is a painful condition and therefore requires drugs that has rapid onset of action. Hence the intent of the authors to formulate fast dissolving tablets of Flurbiprofen using different superdisintegrants to improve the dissolution rate and bioavailability of the drug. Flurbiprofen fast dissolving tablets were prepared using various superdisintegrants and the resultant formulations were characterized for different physical parameters. The results of the statistical analysis carried out by the authors on the various data obtained showed that the use of superdisintegrants to formulate fast dissolving tablets of Flurbiprofen was a good way to enhance bioavailability, dissolution rate and absorption rate of the drug.

Due to the recent advances in novel drug delivery system (NDDS) to enhance safety and efficacy of already existing drugs, the authors decided to formulate fast dissolving Flurbiprofen tablets and study the effect of superdisintegrants on bioavailability of the Flurbiprofen tablets in the research work titled "formulation, evaluation and pharmacokinetics of Flurbiprofen fast dissolving tablets" in the early part of the year 2013. This was to also serve as an addition to the currently available database on studies of fast dissolving tablets which probably began at the middle of the 20th century. Since then various studies have been carried out by several researchers in attempt to formulate various orodispersible tablets of some of the already existing drugs. But only few have been able to attribute the orodispersability and enhanced bioavailability of Flurbiprofen fast dissolving tablets to the incorporation of Crospovidone in their formulations. That is what the authors were able to discover from the evaluations in their own study with similar results having been obtained by Vemura et al (2009) which the authors also cited in their work.

In the introductory part of the research report the authors defined Flurbiprofen as a phenylalkanoic acid derivative which belonged to a group of poorly water soluble drugs and classified as a non-steroidal anti-inflammatory drug whose major indication is in the long-term treatment of chronic rheumatoid diseases. Flurbiprofen being a class II drug is therefore limited in its therapeutic activity due to its slow rate of absorption from the oral route of administration which is currently considered as the gold standard in the pharmaceutical industry.

Based on the above stated limitation, the authors attempted to study the improvement of dissolution rate of Flurbiprofen using the basic approach in the development of fast dissolving

tablets which required the use of superdisintegrants. This might also be based on the fact that most of the chronic rheumatoid disease patients belong to the geriatric population and may suffer from mild hand tremors and dysphasia which makes it difficult to swallow tablets hence the urgent need for fast dissolving tablets of Flurbiprofen in order to enhance the ease of administration and also increase patient compliance.

Several attempts had been made in the past to prepare fast dissolving tablets through various means out of which the authors combined the wet granulation method with subsequent direct compression of the tablets. The composition of the fast dissolving tablets included superdisintegrants e.g. Crospovidone, lubricants e.g. aerosil, taste mask (aspartame), binding agent i.e. starch alongside other excipients. Twelve formulations were prepared with the conventional tablets serving as control. All were evaluated for physical properties, in vitro disintegration time and dispersion time, wetting time, d5rug-excipient interaction, water absorption rate and stability studies. The authors went a step further by carrying out an in vivo crossover study involving six healthy volunteers who received the drug and had their blood sample obtained for HPLC analysis. Statistical analysis was carried out on determined parameters of both conventional and optimized fast dissolving tablets of Flurbiprofen at significance level 0.05 using a paired t-test.

Evaluation of the physical parameters showed that all the tablet formulations passed the requirements of the India Pharmacopoeia, 1996. From the results of the statistical analysis of data obtained from both in vitro and in vivo studies, formulation F6 showed both rapid disintegration time and in vitro dispersion time. This was due to the Crospovidone content of the formulation. The drug release studies also corroborated the finings by showing that increase in super disintegrant (Crospovidone) quantity from 2-8% was a factor. This was similar to the results obtained by Vemura et al as cited by the authors although their result was obtained using 10% Crospovidone in their formulation.

Furthermore, the thermograph of the Differential Scanning Calorimetry studies suggested no significant drug-polymer interaction. It is important to note that the authors did not carry out a drug-drug interaction studies to examine its suitability for concomitant administration with other drugs as many of the patients with chronic rheumatoid disease conditions might be on medications for other ailments. Pharmacokinetic analysis of the plasma obtained suggested increased bioavailability of Flurbiprofen when superdisintegrants are added.

At this juncture, it would be worthy to commend the authors for the good attempt at developing fast dissolving tablets of Flurbiprofen using a minimal concentration of superdisintegrants. The authors' use of tables and graph to explain some of the details did not go unnoticed. However mention must be made of the omission of pharmacodynamics of the fast dissolving tablets of Flurbiprofen which the authors should consider investigating in future. Also, further research to establish the efficacy of these fast dissolving tablets using appropriate clinical studies is recommended. Overall, the authors have done well in updating the use of fast dissolving tablets as a Novel drug delivery system for an important existing anti-inflammatory drug such as Flurbiprofen.

REFERENCES

1) Grri, M., Rangoni, C., Maestraelli, F., Corti, G., Mura, P. (2005). Development of fast developing tablets of flurbiprofen-cyclodextrin complexes. *Drug dev Ind Pharm, Aug, 31(7), 697-707.*

2) http://www.drugs.com/flurbiprofen. Accessed July 7, 2013.

3) Kuchekar, B., S., Badhan, A., C., Mahajan, A., S. (2003). Mouth dissolving tablets; A novel drug delivery systems. *Pharma. Times, 35,7-9.*

4) Shid, S., L., Hiremath, S., P., Borkar, S., N., Sawant, V., A., Shende, V., S., Tote, M., V., Birari, R., B., and Changrani, S., R. Effect of superdisintegrants in rapidly disintegrating flurbiprofen sodium orodispersible tablets via direct compression and camphor sublimation.

5) Watanabe, Y., Koizumi, K., Zama, Y., and Matsumoto, Y. (1995). New compressed tablet rapidly disintegrating in saliva in the mouth using crystalline cellulose and a disintegrant. *Bio. Pharm. Bull, 18(9), 1308-13*

6) Wenat, A., K., Patel, S., M., Patel, S., R., Patel, N., M. (2012). Fast dissolving tablets: A novel approach to drug delivery. *Asian journal of pharmaceutical sciences and research, 2(8).*