Journal of
Formulation Science & Bioavailability

Sengupta, J Formul Sci Bioavailab 2016, 1:1

Opinion Open Access

Importance, Rationality and Requirements of Fixed Dose Combination Dosage Form

Sengupta P*

Professor in the Department of Pharmaceutical Technology, International Islamic University Malaysia, Malaysia

Introduction

Many patients with chronic diseases have two or more co-morbid factors and needs multiple medications. Low patient compliance to the medicines prescribed for self-administered is well established and is particularly problematic in the treatment of chronic diseases. Newer approaches to improve patient compliance can reduce the mortality rate of such conditions.

Improper follow of prescribed dosing regimen reduces the benefits of therapy which leads to under-treatment of a disease. Such poor adherence can results in medication wastage, increases in health-care costs, and drug resistance particularly for infectious diseases. A report from World Health Organization (WHO) on adherence to long-term therapies (World Health Organization, 2003) indicated that the simplicity of the dosage regimen had the greatest influence on patient compliance. Lack of simplicity in self-administered drugs in chronic diseases decreases the patient compliance (World Health Organization, 2003). Fixed-dose combination (FDC) preparations are single finished pharmaceutical dosage form developed with two or more different drugs in a fixed ratio of doses. The development of FDCs is becoming very important from a public health perspective. FDCs are nowadays widely used in the treatment of a various disease conditions. Fixed-dose combination pills are therapy-related discovery developed to simplify medication regimens and so significantly increase compliance. FDC pills have been developed for the treatment of several diseases, being an important component of control of infectious diseases, and have recently been evolved for multiple uses in other conditions as well (World Health Organization, 2002; Wald and Law, 2003). By reducing the number of doses of the drugs, they provide greater patient convenience and compliance. Additionally, simplification of drug handling and supply, lower packing and shipping costs and prevention of short supply of individual components will be of particular value, especially in developing countries. Other notable advantages of fixed-dose combination treatment include synergistic effect and treatment of multiple pathophysiological conditions with a single dosage form.

But, the safety profile of a drug may get altered when it is combined with others. Serious drug interactions can result in an alteration of the pharmacological profile of the drug resulting some less efficacious and others highly toxic. These potential drug interactions should be studied well. A mechanism for adverse drug reactions and interaction study, as well as cost analysis should also be established for all new FDC preparations. Interestingly, more than one-third of all the new drug products introduced worldwide during the last decade were fixed dose combination preparations. Although there are insufficient statistical data in the developing countries, the trend indicates the production and prescription of FDCs.

There are some factors to be considered to establish the rationality for combining different drugs into a single formulation (WHO Technical Report, 2005). Medical considerations are not simple and need to consider whether increased efficacy is accompanied by increased toxicity. The decision regarding marketing approval for a new FDC based on a consideration of the balance between risk and benefit from the medical perspective. Consideration of the bioavailability and bioequivalence study of the drugs in combination is also very important. It is not acceptable if bioavailability is reduced or variable, when compared with that of single drug products, but an interaction between two actives that leads to an increased bioavailability may be one of the advantages that are considered when balancing risk and benefit.

For the approval of a new FDC, it is required to demonstrate all the possible advantages of the new combination against the disadvantages. The demonstration should be based on the existing data and on scientific and medical principles. In some country, the cost of the FDC is compared against the cost of individual dosage form. The improvement in reliability in terms of supply as a result of simplified distribution procedures of the new FDC is also taken into consideration. It can be assumed that improved patient compliance may result from more reliable availability of the FDC than of all of the components as loose combinations of single entity products.

Again, additional problems may arise when two or more drugs are combined. These complexities are mainly related to assay, stability, physicochemical properties, safety and efficacy. If the safety and efficacy of the FDC in humans has not already been established, preclinical testing need be carried out on the drugs in combination to investigate possible additive or synergistic toxicological effects. The preclinical testing should aim to determine both the pharmacological and the adverse reactions that may be expected from combining the drugs during clinical use. As a general rule, preclinical studies for the combination required to be carried out with the drugs in the similar ratio as in the fixed dose combination in question.

***Corresonding author:** Sengupta P, Professor in the Department of Pharmaceutical Technology, International Islamic University Malaysia, Malaysia, Tel: 603 - 6196 4000; E-mail: pinaki@iium.edu.my

Received November 11, 2016; **Accepted** November 17, 2016; **Published** November 21, 2016

Citation: Sengupta P (2016) Importance, Rationality and Requirements of Fixed Dose Combination Dosage Form. J Formul Sci Bioavailab 1: 101.