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Application of SeDeM Expert system in formulation development of effervescent tablets by direct compression

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Amjad Khan [a], Zafar Iqbal [a,*], Zahir Rehman [b], Fazli Nasir [a], Abad Khan [a], M. Ismail [a], Roohullah [a], Akhlaq Mohammad [a]

[a] *Department of Pharmacy, University of Peshawar, Peshawar, Pakistan*
[b] *Ferozsons Laboratories Pvt. Ltd., Nowshera, Pakistan*

Abstract The SeDeM expert system is a pre formulation tool applied for the prediction of the suitability of a material for direct compression. This innovative tool provides an index of good compressibility of the material indicating its aptitude to be compressed by direct compression. In the study the SeDeM expert system has been applied for the prediction of the behavior of the material to be used in the formulation of effervescent tablets by direct compression. Different formulations were developed on the basis of the results of the SeDeM expert system.

Various parameters for the material as per the SeDeM expert system were determined according to their official and reported methods. Powder blend for different formulations was evaluated for their rheological properties while tablets were evaluated for various official and unofficial tests.

Suitability of the material for direct compression was successfully predicted using the SeDeM expert system. Domperidone was found unsuitable for direct compression. During formulation all excipients responded as they were predicted as per the SeDeM expert system. Tablets produced using the resultant formulations were having sufficient mechanical strength, free of premature effervescence and were capable to be scaled up for commercial manufacturing.

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1. Introduction

SeDeM expert system is a pre formulation methodology applied for the formulation development of solid dosage form (Tablets) by direct compression (Pilar et al., 2006). Quality by design ICH-Q8 provides a basis for the SeDeM expert system. It is used for an evaluation of critical quality attributes having an impact on the final product. This system provides a physical profile of A.P.I. and excipients intended to be used

* Corresponding author. Tel.: +92 91 9239619; fax: +92 91 9218131.
E-mail address: zafar_iqbal@upesh.edu.pk (Z. Iqbal).
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and suggests their suitability for direct compression (Johnny et al., 2009). It also points out parameters needing to be improved to get a formulation that can be successfully processed by direct compression i.e., the profile of powder shows its advantages and gaps for their suitability for direct compression (Pilar et al., 2006; Inderbir and Pradeep, 2012).

The SeDeM expert system also calculates the amount of excipients with certain characteristics required for correction of a particular property in order to make the final blend suitable for direct compression. Several parameters have been selected that must be fulfilled by the formulation to ensure successful and robust processing by direct compression technology (Johnny et al., 2012; Josep et al., 2008).

Effervescent tablets are a promising dosage form combining qualities of both solid and liquid dosage forms. These are dissolved or dispersed in water before administration and taken as liquid thus presenting the drug in a palatable liquid form while retaining the properties of a solid dosage form like easy portability, high stability and accurate dose (British Pharmacopoeias, 2008). pH of the liquid formed after effervescence reaction can be controlled in the desired range by a proper selection of the quantities of acids and base. Furthermore, as the drug is administered as a liquid, the whole of it is made available for absorption from GIT (Ashutosh et al., 2008; Harald, 2003).

The main problem with effervescent tablets is their chemical instability exhibited by the premature effervescent reaction. Even trace amounts of the water can initiate the self propagating reaction that continues till the consumption of the whole of the acid and/or base resulting in a complete deterioration of the product (Harald, 2003). Therefore the process of preparation should be carried out in an environment of controlled humidity with a reduced number of steps to minimize material exposure. The method of direct compression is desirable for the preparation of effervescent tablets (Robert, 2001; Yuhua and Diana, 2009) as it involves fewer steps and less material handling and exposure (Harald, 2003). Main problem with the direct compression method is the prediction of material flow and compressibility. Most of the APIs lack sufficient flow and compressibility and requires selecting proper excipients for their formulation by direct compression. A large number of trials should be carried out to obtain formulations with proper rheological properties and compressibility. This makes the process more tedious, time consuming and a lot of material is utilized. The SeDeM expert system can overcome the problem as it develops a database for excipients and an easy selection can be made without extra trials.

The SeDeM expert system has been applied for the prediction of the suitability of different material used in the formulation of effervescent tablets by direct compression. The results predicted by the SeDeM expert system have been confirmed by an analysis of trials of the different formulations.

Various formulations were developed containing the effervescent pair alone and in combination with super disintegrants. Effects of super disintegrant, tablet compression force and tablet surface area have been evaluated.

Domperidone (5-chloro-1-h1-(3-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl)-4-piperidinyl-1,3-dihydro-2H-benzimidazol-2-one) was selected as a model drug. It is a dopamine-receptor antagonist acting peripherally, having no central effects with the elimination half life of 5–7 h (David et al., 1998). According to bio pharmaceutical classification system, domperidone has been classified as a class 2 drug. It is a weak base having a good solubility at lower pH (Nagarsenker et al., 2000). It absorbs well when the whole of the drug is available for absorption in the acidic segment of G.I.T. This can be made possible by administering domperidone as an effervescent tablet.

2. Materials and methods

2.1. Material

Domperidone (Ningbo Sansheng Pharmaceuticals Company, China) was purchased from Medicraft pharmaceuticals, Peshawar. Citric acid anhydrous, tartaric acid and sodium bicarbonate (Merck KGA, Germany) were purchased from sigma chemicals, Karachi. Rest of the excipients (Micro crystalline cellulose (F.M.C. Bio polymers, Ireland), Tablettose (Molkerei Meggle, Germany) and Magnesium stearate (Peter Greven, Malaysia) were a kind gift from Ferozsons Laboratories, Ltd., Nowshera. All the materials were of pharmaceutical grade.

2.2. Methods

2.2.1. Evaluation of material as per SeDeM expert system
Powder material was evaluated for different parameters according to the SeDeM expert system to determine their suitability for direct compression. Some of them were determined experimentally according to the established procedure and some were calculated from experimental values of other parameters (Pilar et al., 2006) as per Table 1.

2.2.2. Determination of basic parameters
The basic parameters of the SeDeM expert system are given as;

- Bulk density
- Tapped density
- Interparticle porosity
- Carr's index
- Cohesion index
- Hausner ratio
- Angle of repose
- Powder flow
- Loss on drying
- Hygroscopicity
- Particle size smaller than 50 μm
- Homogeneity index

2.2.3. Conversion of experimental values (V) to radius value (r) of SeDeM diagram
The numerical values for different parameters of the material obtained by experimental determination were converted into a radius value (r) of the SeDeM expert system diagram. For the conversion of experimental value of each parameter, specific factors were applied (Johnny et al., 2009) as listed in Table 1.

2.2.4. Graphical presentation of SeDeM diagram
SeDeM diagram was built up on the basis of 12 parameters looking as 12 sided polygon (Johnny et al., 2009). Results