Formulation Of Liquisolid Powder Of Fisetin

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Abstract: Fisetin is a polyphenolic compound which is a dietary flavonoid and mostly found in fruits, vegetables, seeds, nuts, tea etc. It faces a major challenge of poor aqueous solubility and poor bioavailability. To improve the dissolution rate, we have prepared liquisolid powder of fisetin. Liquisolid powder, batch F1 to F3 were formulated. Among them formulation F2 has shown good results. It contained, fisetin 0.30g, tween-80 6g, Aerosil 200 5g, and Lactose 3g. Formulation F2 showed very good micromeritic properties such as angle of repose, bulk density and Carr's index. Hence, the study indicated successful development of liquisolid powder of fisetin. The dissolution study showed increase in dissolution rate of fisetin from liquisolid powder as compared to that of pure fisetin.

Keywords: Fisetin, Formulation, liquisolid, Flavonoid

Introduction

Fisetin is a polyphenolic compound which is a dietary flavonoid and mostly found in fruits, vegetables, seeds, nuts, tea etc. It shows very good pharmacological activities such as antioxidant, neurological, antiviral, anticancer (Breast cancer, ovarian cancer, Lung cancer, Colon cancer, Prostate cancer, Oral cancer), cardiovascular, antimicrobial, anti-inflammatory, anti-Alzheimer's and anti-diabetic (treating type 2 diabetes mellitus) activities (Anand *et al.*, 2017; Sharma *et al.*, 2014). It possesses poor aqueous solubility: There are many formulations prepared for this drug such as Self nanoemulsifying drug delivery systems, nanosuspension, complex, liposomes, microspheres, metallic nanoparticles, nanoemulsion, solid dispersion, nanostructured lipid carriers (NLCs) etc (Kumar *et al*., 2019a, 2019b; Garg *et al*., 2017a). For achieving fast and complete drug dissolution, liquisolid technology is advantageous as compared to other techniques used to overcome aforementioned issues (e.g., transformation into soluble amorphization or polymorph, complex formation ,solid dispersion, solid lipid nanoparticles and nanosuspension) (Gavali *et al*., 2011(Garg *et al*., 2017b; Kaur *et al*., 2015; Kaur *et al*., 2017; Kumar Singh *et al*., 2016; Mahesh *et al*., 2014; Renuka *et al*., 2017; Renuka *et al*., 2014; Singh *et al*., 2011; Singh *et al*., 2012b). It is a simple, economical method with an enormous industrial production potential. Liquisolid formulations are free-flowing and compressible powders of drug dissolved in liquid vehicle (Burra *et al*., 2011). The liquisolid powder is a drug solution or dispersion in a non-volatile liquid (such as: Polyethylene glycols (PEG) PEG 200, PEG 400, PEG 600 and polysorbates), which is adsorbed on solid excipients, popularly known as carrier (For example: Microcrystalline cellulose, Aerosil 200) and coating material (Such as: amorphous silicon dioxide, S244FP) (Patra *et al*., 2016; Maharshi *et al*., 2018; Prudhviraj *et al*., 2015; Singh *et al*., 2012a). The final dosage form is powder or compact, afterwards it can be converted into tablet or filled into capsule (Gavali *et al*., 2011)(Jyoti *et al*., 2019; Mohanta *et al*., 2018).

Many drugs having poor aqueous solubility have been successfully delivered through oral route using liquisolid technology (Kapure *et al*., 2013; Yadav and Yadav, 2009; Zhao *et al*., 2011; Bonthagarala *et al*., 2015; Kumari *et al*., 2019; Kumari *et al*., 2020). In liquisolid formulations rapid release rates are obtained. These can be efficiently used for water insoluble liquid lipophilic drugs or solid drugs (Kulkarni *et al*., 2010). Hence, in the present study, we are preparing liquisolid powder of poorly soluble fisetin to enhance its bioavailability.

Materials and Methods

Materials

"Fisetin was purchased from Tokyo Chemical Industries, Japan. Polyethylene glycol 400 (PEG 400) was purchased from Central Drug House (CDH) Pvt., Ltd., Delhi, India. Tween-20 (T-20), Tween-60 (T-60), and Tween-80 (T-80) were purchased from Molychem Pvt., Ltd., Bhadli, Thane, India. Lactose and Aerosil 200 were purchased from Signet Chem., Corp., Pvt., Ltd., Mumbai, India".

Methods

Solubility Studies

Solubility of fisetin was determined in four different non-volatile liquids such as PEG 400, T-20, T-60 and T-80. Fisetin (10mg) was added to each beaker container non-volatile solvent (10mL). The beakers were covered with aluminium foil and sonicated for 48h at 25ºC till the complete fisetin was dissolved. Further fisetin was added in excess into each beaker in order to produce saturated systems containing excess of the drug. The total amount of fisetin was added to each beaker was noted. Centrifugation of solutions was done at 10000*g* for about 15 min. Upon collection of supernatant, suitable dilutions were prepared and absorbance was recorded at 362 nm by using water as blank was measured (Kumar *et al*., 2018; Rajesh *et al*., 2018; Sharma *et al*., 2018, Saggu *et al.*, 2019). In order to nullify the effect of added solubilizer, the reading on UV-Visible spectrophotometer was taken by keeping them as blank.

Formulation of liquisolid powder

Fisetin liquisolid formulation denoted F1 to F3 were formulated using T-80 as liquid vehicle and lactose as solid carrier. Aerosil 200 was used as coating agent. The composition is shows in Table 1. Initially, fisetin (0.3g) was taken in mortar and 6g of tween 80 was added drop wise. Afterwards, the dispersion was mixed homogenously using spatula. Upon complete solubilization of drug in tween 80, varying amount of lactose was added in formulation F1 to F3. Further, Aerosil 200 was added in varying amount as coating material. The mixture was blended for 15 min. using pastel and powder was collected for further use.

Table 1: Formulation of liquisolid powder

Components (g)	F1	F2	F3
Fisetin	0.3	0.3	0.3
Tween 80	6	6	6
Aerosil 200	4.2	5	4
Lactose	2.5	3	3

Evaluation of powder

Angle of repose (AOR)

Fixed funnel method was used to calculate AOR by pouring the known quantity of powder from pre-determined height through a glass funnel on a graph paper. The height and diameter of pile was noted and AOR was calculated using following formula (Gavali *et al*., 2011).

$$Angle\ of\ repose\ (\theta = tan - 1\frac{h}{r})$$

Where,
Θ = Angle of repose
h = height in cm
r = radius in cm
Limits: Θ is 25 to 30 shows excellent flow while 31 to 35 indicates good flow, 36 to 40indicates fair flow and 41 to 45 indicates passable flow (El-Say *et al*., 2010).

Bulk density (BD) and tapped density (TD)

The study was carried out using bulk density apparatus. BD was determined by pouring the powder into a graduated cylinder. The weight of the powder (M) and bulk volume (Vb) was determined (Gubbi and Jarag, 2009). Calculated the initial bulk density.

$BD = m/v$b
Where BD= bulk density
M = weight of powder in gram
Vb = Powder's bulk volume
The powder was tapped for a fixed time. Measurement of the tapped volume of powder (Vt) present in the cylinder as well as weight (M) of the powder was noted (Sanjesh *et al*., 2019). The tapped density was calculated using formula.

$$Dt = M/vt$$

Where,
Dt = tapped density
M = weight of powder in gram
Vt = tapped volume of powder

Carr's index (CI)

It shows about compaction properties of blend and calculated using formula given below -

$$CI = \frac{tapped\ density - bulk\ density}{tapped\ density} \times 100$$

Hausner's ratio (HR)

$$HR = \frac{tapped\ density}{bulk\ density}$$

Dissolution study

In vitro release of liquisolid powder is carried out using 0.1 N HCL, Type I apparatus, 900 mL medium volume at 37 ºC ± 2 ºC. The study was carried out for 60 minutes. At different time intervals, 5 mL aliquots were withdrawn from dissolution medium. After appropriate dilutions and filtration, the samples were analyzed at 362 nm using UV-Visible spectrophotometer. The amount of drug released was calculated using the calibration curve method (Kavitha *et al*., 2011).

Results

Solubility studies

Fisetin has shown maximum solubility among all the solubilizers in tween 80 (80%) followed by tween 20 (65%), tween 60 (22%), PEG 400 (14%). Hence, it was used as liquid vehicle in the formulation.

Micrometric parameters

The powder flow properties of liquisolid formulation for F1 to F3 are shown in Table 2. Among them, F2 showed better results than F1 and F3. Hence, it was subjected for dissolution studies.

Table 2: Micrometric parameters of formulation

Formulation	AOR (°)	BD (g/cm^3)	TD (g/cm^3)	CI	HR
F1	33.54	0.51	0.67	9.12	1.31
F2	22.98	0.60	0.62	3.23	1.03
F3	31.55	0.64	0.76	15.79	1.19

Dissolution studies

The results of dissolution studies indicated 80% drug release in 15 minutes whereas only 12% drug release was observed from unprocessed fisetin. The results are shown in Figure 1.

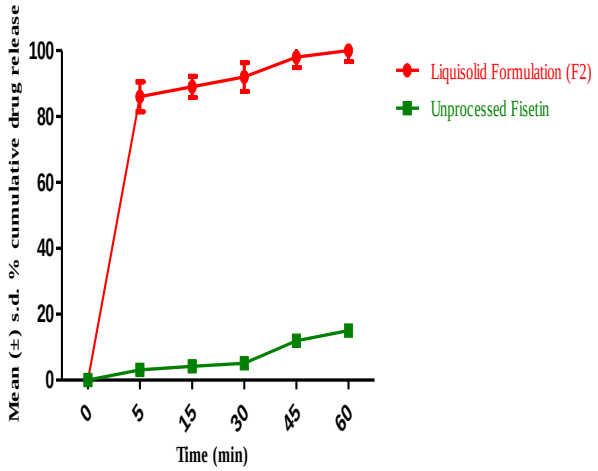

Fig. 1: Dissolution studies

Conclusion

It is concluded that liquisolid formulation of fisetin are successfully formulated with very good flow properties.

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