Department of Pharmaceutical Sciences[1], University of Florence, Aboca s.s., Loc. Aboca[2], Sansepolcro, Arezzo, Italy

Evaluation of the dissolution behaviour of some commercial herbal drugs and their preparations

V. Taglioli[1], A. R. Bilia[1], C. Ghiara[2], G. Mazzi[1], V. Mercati[2] and F. F. Vincieri[1]

Dissolution rates are routinely performed with synthetic drugs, however, in the field of herbal drugs (HD), their preparations (HDP) and herbal medicinal products (HMP) this crucial property is generally not investigated. According to the European Pharmacopoeia, we have evaluated the dissolution behaviour of capsules containg various herbal drugs (*Passira*, *Senna*, *Ginkgo*) and some of their commercial dried extracts, manufactured with different methods, by analysis of their active components or marker constituents. Adequate dissolution behaviours of the flavonoids of *Ginkgo* were obtained for all preparations, while for both *Passiflora* and *Senna* only the extracts showed complete dissolution of the marker flavones and sennosides, respectively, in the investigated media.

1. Introduction

The absorption of orally administered drugs in solid forms such as tablets, capsules and suspensions as well as suspensions intramuscularly administered is largely dependent on the active components being in the dissolved state. In many instances, dissolution rate, or the time it takes for the drug to dissolve in the fluids at the absorption site, is the rate-limiting step in the absorption process. Consequently, this rate can affect the onset, intensity and duration of response and can control the overall bioavailability of active components from the dosage form [1].

In general, dissolution rate can be increased by decreasing the particle size of the drug. Even so, in some cases an inverse relationship of particle size to dissolution has been noted due to the surface properties of the drug such as surface charge and/or agglomeration, resulting in a lower effective surface area to the solvent due to incomplete wetting or agglomeration [2].

Dissolution tests are routinely performed with synthetic drugs, however, in the field of herbal drugs (HD), their preparations (HDP) and herbal medicinal products (HMP) this crucial property has usually not been investigated.

The aim of this work was to investigate the "*in vitro*" bioavailability of the active components or marker constituents of different herbal drugs (*Passiflora*, *Senna*, *Ginkgo*) and some of their commercial dried extracts manufactured by different methods. All drugs are generally marketed in the form of hard gelatine capsules. Currently, phytochemicals destined for oral intake are generally marketed world-wide as solid forms. This is due principally to the better stability of both herbal drug powders or dried extracts obtained by different manufacturing technologies and containing different excipients, many of which are covered by patents.

Two piece hard gelatine capsules were chosen as standard formulation due to the specific situation in Italy and most of Europe, where hard gelatine capsules are the easiest delivery form to be manufactured. These can be made by filling with a certain amount of HD powder or dried extract and closing the commercially available two piece hard gelatine. Due to the easy way of preparation, these products are also made as galenical products by pharmacists in their own laboratories.

2. Investigations, results and discussion

The products tested were formulated as standard commercial two piece hard gelatine capsules by using HD powders or dried extracts titled in active or marker constituents (Table). Quantitative measurements of the constituents were performed according to UV-Vis photometric measurements of vitexin for *Passiflora*, rutin for *Ginkgo* and sennoside A for *Senna* as reference compounds. All the samples were introduced in hard gelatine capsules with a constant amount of active or marker constituents. Experiments were run in triplicate.

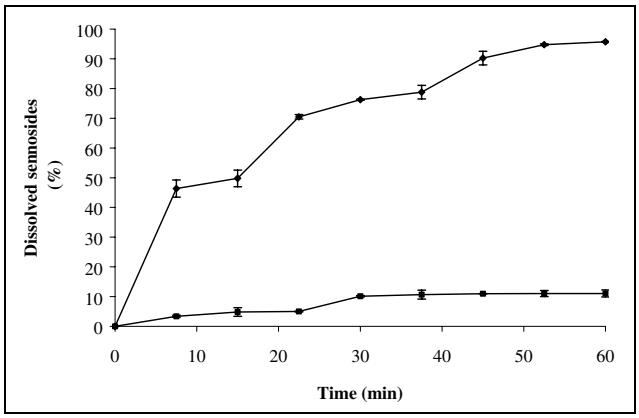

Fig. 1: Dissolution behaviours of *Senna* preparations. ◆ freeze-dried extract; ■ powder extract

Table: Lots and markers or active constituents content of HD powders and dried extracts used for the dissolution tests

Herbal drug	Powder		Freeze-dried		Granulate		Passoflo2-LMF	
	Lot.	%	Lot.	%	Lot.	%	Lot.	%
Ginkgo	98/13261/1-9705966/1	0.74	8G043	2.47	64033	2.48		
Passiflora	8237	2.26	62995	9.28			8L3476	5.5
Senna	8H0355	2.18	65867	0.62				

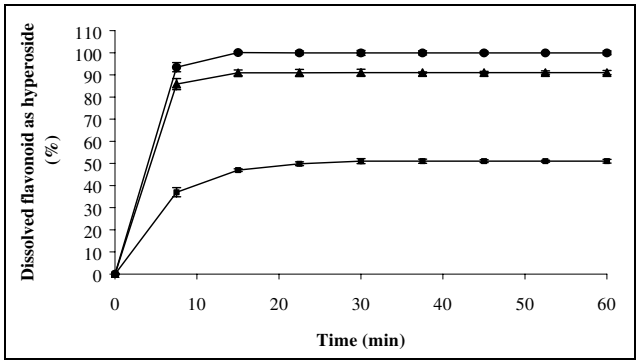

Fig. 2: Dissolution behaviours of *Passiflora* preparations. ◆ freeze-dried extract; ● Passoflo2; ■ powder extract

Dissolution rate profiles of *Senna* preparations are reported in Fig. 1. HD powder and freeze-dried extract gave very different dissolution curves and the quantity of sennosides released from the HD powder represent only 1/10 of the total content. Dissolution properties of the dried extract were very favourable: after 7.5 min the release of sennosides was about 30% and was almost complete by 60 min (95.7%).

Dissolution rate profiles of *Passiflora* preparations are reported in Fig. 2. The dissolution curves of the purified extract Passoflo2-LMF® and the freeze-dried extract can be considered "*in vitro*" quasi-equivalent. The release of flavonoids from both preparations reached nearly 100% by 10 min, while the powder reached a release of about 50% in the same time, but no further increase was found during the following 50 min of analysis. Dissolution rate profiles of *Ginkgo* preparations are reported in Fig. 3. The best dissolution profile was found with the freeze-dried extract, where after about 15 min 100% of flavonoids were released. However, from the results obtained, both powder and granulate should be considered "*in vitro*" quasi-equivalent to freeze-dried extract.

From our data it is clear that the prior evaluation of the dissolution rate is a fundamental step to establish the best HD preparation to be used for capsules. It is clear that also in the field of herbal drugs and their formulation, the dissolution profile of the different samples must be evaluated during the development of a pharmaceutical dosage form to assure quality and efficacy and so to guarantee the therapeutic effect.

The marketed HD powders are used as alternative and less expensive preparations to the extracts. Thus, they do not require additional excipients in the formulation and show sufficient pharmaceutical qualities such as resistance to the humidity, stability, gliding properties. This is true for capsules containing *Ginkgo* powder, which showed an adequate dissolution profile similar to that of other preparations. However, in the case of capsules of *Senna* powder, which are generally marketed in this pharmaceutical form, the "*in vitro*" bioavailability was very different to that of the extract.

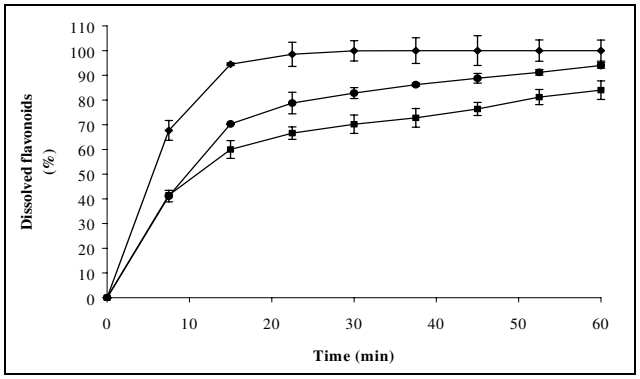

Fig. 3: Dissolution behaviours of *Ginkgo* preparations. ◆ freeze-dried extract; ● granulate extract; ■ powder extract

Furthermore, dried extracts are generally considered a better form, even if they can give agglomerations during the dissolution analysis, which can result in a lower effective surface area to the solvent due to incomplete wetting or agglomeration. Furthermore, all the marketed extracts may not be equivalent. For these reasons, a dissolution profile should always be performed because dissolution is a prerequisite for absorption in the gastrointestinal tract and hence for the good bioavailability.

Thus, from the *Passiflora* and *Senna* preparations, only the extracts show good "*in vitro*" biopharmaceutical proprieties with respect to the drug powders, even if the results showed different release curves.

It is important to emphasize the relevance of the formulation for maximizing absorption. Thus, the efficacy of certain herbal extracts has recently become a major issue. In conclusion, formulation techniques to improve biovailabilty should be maximized to produce optimal efficacy.

3. Experimental

3.1. Materials

All the herbal drug powders and dried extracts are listed in the Table. They were all commercial samples from Aboca s.s. (Loc. Aboca, Sansepolcro, Arezzo, Italy). Dried extracts contained no excipients. Vitexin, rutin and sennoside A analytical samples were purchased from Extrasynthese (Genay, France). Hard gelatine capsules were purchased from Galeno srl Italia, Lot. 01905 prod. 2316.

3.2. Sample preparations

The following capsules were prepared: 100 mg of *Senna* powder and 351.6 mg of *Senna* freeze-dried extract; 100 mg of *Passiflora* freeze-dried extract, 410.6 mg of *Passiflora* powder and 168.4 mg of Passoflo2-LMF®; 100 mg of *Ginkgo* freeze-dried extract, 333.78 mg of *Ginkgo* powder and 99.59 mg of *Ginkgo* granulate.

All analyses were performed in triplicate and the dissolution media were evaluated by UV-Vis spectrophotometer using suitable λ every 7.5 min during 60 min.

3.3. Methods

The apparatus used in the present investigation was a paddle apparatus having the same characteristics as that described in the European Pharmacopoeia [3]. A Sotax AT 7 dissolutor instrument was used equipped with a peristaltic pump (Ismatec® ENCO S.R.L. Venezia Italia), and consisting of a cylindrical vessel with a nominal capacity of 1000 ml with a stirrer having of a vertical shaft at the lower end of which is attached a blade. The upper part of the shaft was connected to a motor provided with a speed regulator and the stirrer rotation was 50 RPM (10 ml/min). A water bath maintained the temperature of the dissolution medium at 37 ± 0.5 °C.

The dissolution rate of the active components was estimated by means of a UV-Vis Lambda 12 Perkin Elmer spectrophotometer instrument at the appropriate wavelenght: i.e. 515 nm for *Senna*, 340 nm for *Passiflora*, 370 nm and 210 nm for *Ginkgo*. These wavelengths were selective to detect sennosides, which represent active constituents of *Senna* [4] and flavonoids of *Passiflora* and *Ginkgo*, which represent the marker constituents [5, 6].

The software system to obtained the dissolution behaviours was a PEDS (Perkin Elmer Dissolution System).

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Vania Taglioli
Department of Pharmaceutical Sciences
via G. Capponi 9
50121 Florence
Italy
vania.taglioli@unifi.it