JPet®

The First Jelly for Pets

Evaluation of JPet® disintegration profile

ABSTRACT: Rapid and complete disintegration of the dosage form is a prerequisite for active ingredient dissolution and absorption and thus an important parameter for bioavailability of oral use formulations. JPet® are complementary feeds with patented formulations in jelly form. For the evaluation of the disintegration profile a disintegration test was performed in compliance to European Pharmacopoeia prescriptions. Soft capsules (Softgels) are the closest pharmaceutical form to JPet® formulas in terms of composition. The disintegration kinetic of a softgel capsule could be assimilated to the disintegration kinetic of JPet® matrix, in relation to the gelatin content. The test result related to the 1g JPet® BASE MATRIX confirm a fully compliance to the softgels requirement as defined by Ph. Eur. and BP, with a disaggregation time under 30 minutes. Results of the examinated JPet® formulas are consistent with the physiological release and absorption of nutrients in the pets intestine, suggesting that the availability of the ingredients is fully guaranteed for each developed formula with JPet® patented technology process and formulas.

INTRODUCTION

Rapid and complete disintegration of the dosage form is a prerequisite for active ingredient dissolution and absorption and thus an important parameter for bioavailability of oral use formulations.
The disintegration test contributes to an overall evaluation of the formulation, in terms of availability of the ingredients and effect onset time.
The formulation is considered as disintegrated when it is dissolved or has disaggregated into numerous particles in a standard medium at defined condition. The time needed to achieve complete disintegration of the pharmaceutical form is measured. Water or artificial simulated gastric fluid of fixed temperature (usually for human use pharmaceutical forms 37°C, for veterinary pharmaceutical forms 38,5° should be considered as reference temperature) serves as disintegration medium. The test conditions should generally mimic the physiological environment as closely as possible.[1]

THE DISINTEGRATION TEST ACCORDING TO EUROPEAN PHARMACOPOEIA

A disintegration apparatus is made by a 1L low-form cylindrical beaker, a heating system that keeps the temperature at 37 ± 2°C, a basket-rack assembly, and a device to move the basket-rack assembly vertically. Two types of basket-rack assembly are described: apparatus A and apparatus B. Apparatus A is described in all major pharmacopoeias: European Pharmacopoeia (Ph Eur), BP, USP and Japanese Pharmacopoeia (JP); whereas apparatus B is described only in the Ph Eur, BP, and the Dietary Supplements chapter of the USP, where it is required for testing tablets and capsules more than 18 mm in length. When required, disks are providing enough pressure to prevent floating of the tablets can be used. The detection of the disintegration time is usually determined visually, when all of the dosage forms except insoluble fragments of coating and/or, in case of capsules, capsule shells are a soft mass with no firm palpable core.[5] Disintegration times vary between different pharmaceutical forms types. (Table 1)

Table 1 Compendial disintegration tests for different dosages forms of veterinary interest:

DOSAGE FORMS	USP General Chapter[3]	USP Dietary Supplements Chapter[3]	Ph Eur[1] and BP[2]	JP[4]
Uncoated tablets	Using water or specified medium. Disks used if proscribed by the Individual monograph.	Using water or specified medium with a 30-min time limit. Disks used if proscribed by the individual monograph.	Using water as the medium. 15 minute time limit. Disks are used	Using water or specified medium and a 30-min time limit unless otherwise specified. Disks used if proscribed by the individual monograph.
Plain-coated tablets	Same as uncoated	Same as uncoated, but sugar-coated tablets should be immersed in water for 5 min at room temperature before the start of the test.	For tablets other than film-coated tablets, use water with disks for 60 min unless otherwise justified or authorized. If any of the tablets fails to disintegrate, repeat with six more tablets using 0.1 M HCl. For film-coated tablets, use the same procedure but for 30 min unless otherwise justified or authorized.	Same as uncoated

Table 1 Continued:

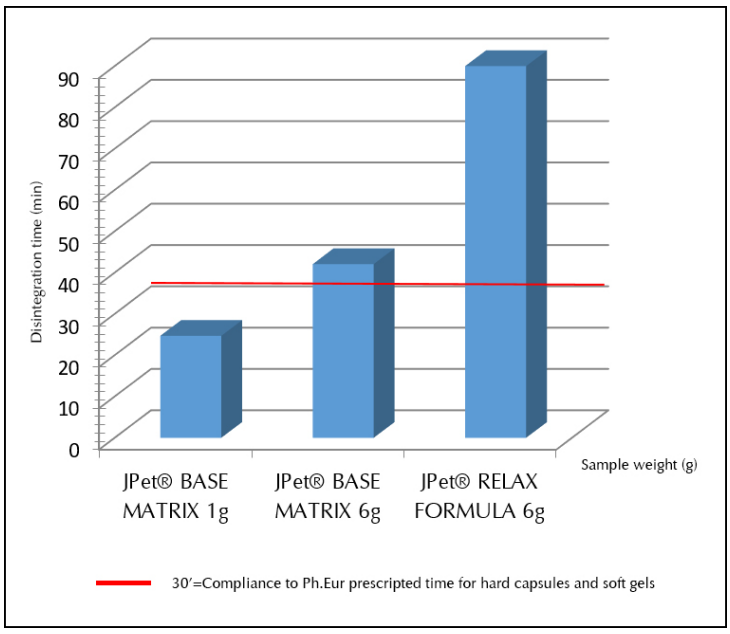
DOSAGE FORMS	USP General Chapter[3]	USP Dietary Supplements Chapter[3]	Ph Eur[1] and BP[2]	JP[4]
Delayed release tablets	One-hour acid stage with SGF, followed by 1-h SIF stage without disks. In case a sugar coating is present, immerse in water for 5 min at room temperature.		Two-hour acid stage (or other time duration if justified or authorized but not less than 1 h) with 0.1 M HCl without disks followed by an 1-h stage in phosphate buffer pH 6.8 R with disks.	Two-hour stage in first fluid for disintegration followed by 1-h stage in the second fluid for disintegration.
Soluble tablets			Using water at 15°C-25°C for 3 min.	
Hard capsules	Same as uncoated tablets, but with a removable wire cloth attached to the surface of the upper plate of the basket.	Similar to the General Chapter but using 0.05 M acetate buffer at a pH of 4.5 as the immersion medium, and with a 30-min time limit.	Using water as the medium. When justified and authorized, 0.1 M HCl or artificial gastric juice may be used. If the capsules float on the surface of the water, a disk may be added. A 30-min time limit, unless otherwise justified and authorized	Using water or specified medium and a 20-min time limit unless otherwise specified. Disks used if proscribed by the individual monograph.
Uncoated soft shell capsules (SOFT GELS)	Same as hard capsules	A rupture test is performed in water using USP type II dissolution apparatus.	Similar to hard capsules but disks are to be used even if the capsules do not float. In case the fill liquid attacks the disks, they may be omitted.	Same as hard capsules

JPet ® DISINTEGRATION TEST

JPet® is a totally new patented jelly formulation, orally use, based on gelatin, without added sugar. Referring to its characteristic composition gelatin-based, JPet® formulations are comparable to SOFT CAPSULES requirements as defined in Ph. Eur.: "Soft capsules have thicker shells than those of hard capsules. The shells consist of a single part and are of various shapes. Soft capsules are usually formed, filled and sealed in one operation, but for extemporaneous use the shell may be prefabricated. The shell material may contain an active substance. Liquids may be enclosed directly; solids are usually dissolved or dispersed in a suitable vehicle to give a solution or dispersion of a paste-like consistency. There may be partial migration of the constituents from the capsule contents into the shell and vice versa because of the nature of the materials and the surfaces in contact."
Soft capsules comply with the test for disintegration of tablets and capsules (2.9.1 Ph. Eur. section): "Use water R as the liquid medium. When justified and authorised, 0.1 M hydrochloric acid or artificial gastric juice R may be used as the liquid medium. Add a disc to each tube. Liquid active substances dispensed in soft capsules may attack the disc; in such circumstances and where authorised, the disc may be omitted. Operate the apparatus for 30 min, unless otherwise justified and authorised. If the capsules fail to comply because of adherence to the discs, the results are invalid. Repeat the test on a further 6 capsules omitting the discs."
JPet® is a new, smart and tasty way to supplement the diet of dogs and cats with nutritional principles like :vitamins, minerals, botanical extracts and selected nutrients for specific needs. All the formulations share a BASE MATRIX where different active nutraceutical ingredients are added.

A disintegration test of 1g Jpet® BASE MATRIX was performed (38,5°C - HCl 0,1M) resulting in a disintegration time of 24 minutes and 07 seconds. The same test was performed on 6g JPet® BASE MATRIX with bone shape (38,5°C - HCl 0,1M) resulting in a disintegration time of 42 minutes and 06 seconds. (LabAnalysis srl-Via Europa,5-27041 Casanova Lonati - PV-Italy-09.02.18) A disintegration test of 6g JPet® RELAX FORMULA (BASE MATRIX with dry extracts of Valerian roots, Californian poppy, Passion flower and Thryptophan) was performed (37°C-water medium) resulting in a disintegration time of 90 minutes. (LabAnalysis srl-Via Europa,5-27041 Casanova Lonati-PV-Italy-07.09.17) (Graphic 1)

Graphic 1 JPet® disintegration profiles



CONCLUSIONS

Although in the pharmaceutical field it does not exist a specific disintegration test for jelly made formulas, especially with a direct application to nutraceutical veterinary complementary feeds, the closest one should be considered the prescribed test for soft capsules (softgels), common among formulations intended for human use. A softgel is an oral dosage form for medicine similar to capsules; it consist of a gelatin based shell surrounding a liquid fill. Softgel shells are a combination of gelatin, water, opacifiers and a plasticiser such as glycerin or sorbitol. The ability of gelatin gels to melt at body temperature has obvious significance for hard and soft capsules. The melting point depends on many factors, including concentration, molecular weight, pH, thermal history and additives. The disintegration kinetic of a soft capsule thicker shell could be assimilated to the disintegration kinetic of JPet® matrix, in relation to the gelatin content.

The test result related to the 1g JPet® BASE MATRIX confirm a fully compliance to the soft capsules requirement as defined by Ph. Eur. and BP (Table 1), with results clearly under the time fixed limit.

The results referring to the 6g JPet® BASE MATRIX and 6g JPet® RELAX FORMULA define different disaggregation profiles, not linear with the findings related to the 1g JPet®BASE MATRIX.

These findings are related to different factors:

- 6 grams is an higher value compared to those normally found in veterinary formulations, considering that maximum tabs average weight, for dogs and cats, is around 2 grams.
- At the present stage, test for high weight pharmaceutical formulations does not exist.
- JPet® BASE MATRIX 's behaviour resembles a non newtonian fluid once dissolved over 35°C temperature, and this could influence the dissolution profile which is non linear. As a gelatin gel is warmed , the rigidity decrease and then disappears relatively rapidly, but the melting point and setting point (gelation temperature) do not coincide, even when the heating and cooling rates are very slow.[6]
- Results obtained testing JPet® RELAX FORMULA, compared to those of JPet® BASE FORMULA, are related to the high content of active substances, which slows the dissolution profile.

Results of the examinated JPet® formulas are consistent with the physiological release and absorption of nutrients in the pets intestine, suggesting that the availability of the ingredients is fully guaranteed for each developed formula with JPet® patented technology process and formulas.

REFERENCES:

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