Doc. No.: AYD 07 (24468) WC
January, 2024

BUREAU OF INDIAN STANDARDS

भारतीय मानक मसौदा

होम्योपैथी में प्रयोग हेतु ग्लोब्यूल्स (Globules) – विशिष्टि

Draft Indian Standard

Globules for use in Homoeopathy – Specification

Homoeopathy Sectional Committee, AYD 07 **Last Date of Comments: 24.03.2024**

FOREWORD

Globules, the small scattering beads are the homoeopathic means of conveyance in which medicines are mixed and given for their internal administrations either by oral or olfaction. These are comparatively inert and the most commonly used vehicle for dispensing homoepahtic medicines by the retailers and by the practitioners.

Globules are particularly popular with children for whom homoeopathic drops are unsuitable due to their alcohol content. Children usually don't mind taking the little sugar pellets, whereas they often refuse to take other medicine. Globules are very light and can therefore be transported very easily.

As Medical Science progress is increasing day by day, likewise the side effect of allopathic medicines are also being seen in the world. Looking to the adverse effect of allopathic medicines, population of this era is moving towards the Homoeopathic or alternative medicines, because of quite low adverse effect. Therefore, demand of homoeopathic medicines is increasing day by day and looking to the demand of Homoeopathic drugs, demand of globules is also increasing. Due to continuous demand, there is possibilities of adulterations as in manufacturing sugar globules basic raw material is sugar which is easily available in each and every part of the country.

The standard is being brought out for the use of drug manufacturers, researchers, academicians, students, and clinical practitioners.

In the formulation of this standard, significant assistance has been derived from the Indian Standards published by the Government of India. Inputs have also been derived from the information available in the public domain in print and electronic media including authoritative books like HPI, Indian, U.S. (USP), French and other Pharmacopoeias.

In the formulation of this standard due consideration has been given to the provisions of the Food Safety and Standards Act, 2006 and Drugs & Cosmetics Act, 1940 and Rules framed thereunder. However, this standard is subject to the restrictions imposed under these rules and regulations, wherever applicable.

For the purpose of deciding whether a particular requirement of this standard is complied with, the final value, observed or calculated, expressing the result of a test shall be rounded off in accordance with IS 2 :2022 'Rules for rounding off numerical values (*second revision*)'. The number of significant places retained in the rounded off value shall be the same as that of the specified value in this standard.

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Draft Indian Standard

Globules for use in Homoeopathy – Specification

1 SCOPE

This standard prescribes the description, preparation, production, and test methods, including packing and storage for globules used for dispensing Homoeopathy medicines. It also includes medicated globules.

2 REFERENCES

The following standards contain provisions which through reference in this text, constitute provisions of this standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below:

IS No.	*Title*
IS 15279: 2003	Sugar and Sugar Products- Methods of Test
IS 6287: 1985	Methods of Sampling And Analysis For Sugar Confectionery
IS 1070 : 2023	Reagent grade water (Fourth Revision)
IS 10146: 1982	Polyethylene for its Safe Use in Contact with Foodstuffs, Pharmaceuticals and Drinking Water

3. Terminology

For this document, the following terms and definitions apply.

3.1 Globules

Globules, also called pellets or pillules, are made of pure sucrose, lactose or other appropriate polysaccharides or suitable excipients.

4. Requirements

4.1 Description

4.1.1 Globules are formed into small globular masses of different sizes, designated according to the diameter of ten (10) globules measured in millimeters (Ref. HPUS).

4.1.2 They possess a suitable mechanical strength to resist handling without crumbling or breaking.

4.1.3 They are intended for impregnation or coating with one or more homoeopathic preparations (Ref. BP).

4.1.4 Globules made of lactose will absorb dilutions containing water better than those made of sucrose.

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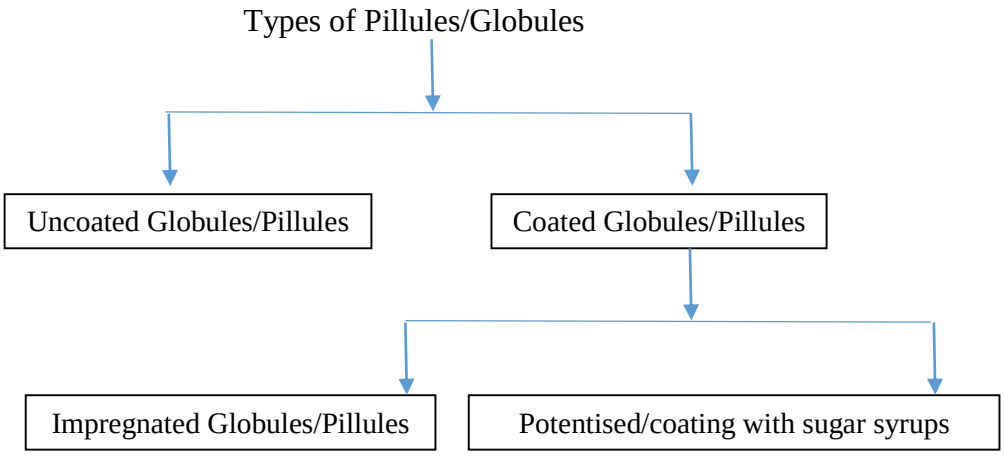
4.1.5 All globules should be made of the pharma grade materials, should be perfectly white and odorless, and should be able to withstand all the tests prescribed for sucrose and/or lactose (Ref. HPUS).

4.2 Size: Standard sizes are as follows:

Sl. No.	Types of Globules	Size	Size in mm
a.	Very Small Globules	10	0.9 - 1.1 mm
b.	Small Globules	20	1.8 - 2.2 mm
c.	Regular Globules	30 40	2.7 - 3.3 mm 3.6 - 4.4 mm
d.	Large Globules	60	5.4 - 6.6 mm

4.3 Types: Based on coating/medication



4.4 Production of Globules: (Ref- BP/EP/GHP-method 39a-c):

4.4.1 Potentized/sugar syrup coated Pillules: It is prepared by coating with a syrup made from homoeopathic preparations either potentised or mixed with sucrose syrup. For coating, use homoeopathic stocks and / or a syrup made from 64 parts of sucrose and 36 parts of purified water. (Note: Range for concentration of sugar syrup 57-64%)

4.4.2 Coated Globules/Pillules: To prepare 100 parts of coated homoeopathic pillules, the pillules are coated with the syrup using one of the following procedures, depending upon the type of homoeopathic preparation used.

a) Aqueous dilutions:

Mix 1 part of an aqueous preparation* with 9 parts of the syrup and potentise by succussion; evenly apply the mixture to (100 - x) parts of pillules (where x is the mass of sucrose in the syrup). The potency of the coated homoeopathic pillules corresponds to the potency of the liquid preparation used for coating. The aqueous fraction of the syrup should be removed at a temperature not exceeding 40 ºC, using constant motion to keep the globules from aggregating before they have dried completely.

(Note: *For aqueous preparation follow the method as per GHP Methods 5b/ 8b/33/37/51)

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b) Triturations

Mix 10 parts of a trituration with 20 parts of the syrup; evenly apply the mixture to (l00 - x- y) parts of pillules (where x is the mass of sucrose in the syrup and y is the mass of lactose monohydrate in the incorporated trituration). The potency of the coated homoeopathic pillules corresponds to the potency of the trituration used.

c) Mixtures

Unless otherwise justified and authorised, prepare a mixture obtained from 10 parts of a liquid preparation (obtained from aqueous preparations, triturations or aqueous dilutions of glycerol macerates) and 90 parts of the syrup, adding sufficient purified water to evenly apply the mixture to (100 - x - y) parts of pillules (where x is the mass of sucrose in the syrup and y is the mass of lactose monohydrate in the incorporated triturations). The potency/potencies of the coated homoeopathic pillules correspond to the potency/potencies of the individual preparations used in the mixture.

4.4.3 Impregnated Globules or Pillules: It is prepared by impregnation of Pillules with one or more liquid homoeopathic preparations. They are intended for sublingual or oral use.

The impregnation process takes place using liquid preparations containing ethanol usually at a concentration of at least 68% v/v (BP/EP) or 70%v/v (HPUS) according to either of the following approaches:

- in proportions of 1 mass part of liquid to 100 mass parts of Pillules
- in proportions of 1 volume part of liquid to 100 mass parts of Pillules

(NOTE: In alcoholic liquid attenuations, the globules are medicated by placing them in a vial and adding the liquid drug attenuation in the proportion not less than 1% v/w, and shaking to obtain a uniform medication. The medicated globules are dried at temperature not exceeding 40°C-HPUS)

4.4.4 Pillules for capsule: The Medicated spheroids are solid products with a diameter not exceeding 2.8 mm. Mini-granules are spheroids with a diameter between 1.0 mm and 2.8 mm, and generally coated. The mini-granules can be obtained by agglomeration accompanied or followed by an operation intended to make them spherical, using various processes such as assembly in a turbine or extrusion. The mini-granules obtained consist of auxiliary substances and of one or more active principles either dispersed in the mass or fixed by impregnation. The auxiliary substances used must be non-toxic under the intended conditions of use; these are in particular: natural polymers, sugars, polyols, waxes, authorized colouring materials, and sometimes flavouring substances.

5. TEST METHODS

5.1 Description: White colored, Spheroids (HPI)

5.2 Solubility: Entirely soluble in water. Insoluble in alcohol. (HPI/BP/EP)

5.3 No. of globules or pillules /g: Weigh about 1 gram of globules and calculate number of globules/g:

$$\text{Number of globules/g} = \frac{\text{Number of globules}}{\text{Weight of globules (g)}}$$

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5.4 Size: Variation in diameter NMT ± 10% (As per HPI). Measure the diameter of 10 globules using Vernier Caliper and calculate the average diameter.

$$\text{Average size of globules (mm)} = \frac{\Sigma \text{ diameter of globule (mm)}}{\text{Number of globules}}$$

5.5 Fineness

Not less than 90% m/m of the pillules are between the lower and upper limits of the corresponding category as indicated in Table.

Table - Classification of pillules according to their mass and size

Category	Number of Pillules for homoeopathic preparations	Mass (g)	Fineness (µm)
1	470 - 530	1.0	1000 - 1600
2	160 - 333	1.0	1400 - 2000
3	110 - 130	1.0	1800 - 2500
4	70 - 90	1.0	2000 - 2800
5	40 - 50	1.0	2500 - 3350
6	16 - 30	1.0	3150 - 4500
7	10	0.9-1.1	4000 - 5600
8	5	0.9-1.1	5600 - 6700
9	3	0.9-1.1	7100 - 8000
10	2	0.9-1.1	8000 - 9500

Note: for categories 7-10, the mass is obtained by weighing the specified number of pillules.
(Note: If the test for fineness is carried out, the test, for uniformity of mass need not to be carried out and vice versa) (As per EP/BP/GHP)

5.6 Uniformity of mass

Carry out the test using 20 pillules to constitute 1 unit. Weigh individually 20 units taken at random and determine the individual and average masses. Not more than 2 of the individual masses deviate from the average mass by more than 10% and none deviate by more than 20% (As per BP/EP).

5.7 Identification test

5.7.1 Solution Z: Dissolve 10 g of inert globule (uncoated/ nonmedicated globule) in purified water and makeup the volume to 100 mL. The solution is clear and colorless.

5.7.2 Add 3 mL of tollens reagent to 3 mL of Solution Z and boil it. A black precipitate (lactose) develops.

5.7.3 Add 3 mL of alkaline cupric tartrate SR reagent to 3 mL of Solution Z and boil it. Observe the formation of an orange precipitate.

5.7.4 Add some indolil acetic acid crystals to 5 mL of hydrochloric acid and five drops of Solution Z. Stir it. Let it rest. A violet color develops (Sucrose).

5.7.5 Add 6 mL of 0.5 Msulphuric acid to 4 mL of Solution Z and heat for a minute, cool it down and neutralize on litmus paper with Sodium hydroxide (8% m/v NaOH in water). Add 5 mL alkaline cupric tartrate SR and boil it for a minute. It must produce brick red precipitate. (As per Brazilian HP)

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5.7.6 Optical rotation

Sample solution: Transfer 20 g to a 200 mL volumetric flask, add 160 mL of water, shake to dissolve the sucrose, add water to volume, and mix. Pass the solubilized sucrose solution by vacuum filtration through fine filter paper.

Acceptance criteria: 65.9° to 67°, based on sucrose ($C_{12}H_{22}O_{11}$) content, calculated on the dried basis (applicable only for sucrose globule).

5.7.7 Starch tests (As per USP) (wherever applicable based on production method)
Analysis: Add iodine TS to the Sample solution Z.
Acceptance criteria: A violet to deep blue color is produced.

5.8 pH (10% w/v in water)

Dissolve 10 g of inert globule (uncoated/ non-medicated globule) in purified water and makeup the volume to 100 mL. pH would be between 5.0 to 7.0 (As per Brazilian HP).

5.9 Loss on drying (As per USP)

Analysis: Take 2 g sample and Dry at 105°C for 4 h.
Acceptance criteria: NMT 4.0% w/w.

5.10 Assay

5.10.1 Sugar content in Globules: It should not be less than 99% of the claimed amount as per the test specified in IS 15279.

5.10.2 Lactose Content in Globules: It should not be less than 94% (w/w) by HPTLC of the claimed amount.

5.11 Impurities (Residue on ignition)

Limit: Not more than 0.25% w/w.
Take 2 g sample and ignite at temperature of 700 ± 25°C. (As per USP)

5.12 Impurities (Foreign matter)

Globules should not contain any of these substances (HPI):
a) Kaolin, b) Chalk, c) Talc, d) Flavor, e) Glycerin, f) Antioxidants, g) Animal dander, h) Inorganic and synthetic whitening agents. Prepare a 5 % w/v Solution A using powdered globules in water and test.

a) Kaolin test	Take 5-10 mL of Solution A in conical flask, add small amount of dilute ammonia solution and allow to stand for 5 min. No white precipitate is observed.
b) Chalk test	Take 5-10 mL of Solution A, add small amount of dilute ammonia oxalate solution and allow to stand for 5 min. No white precipitate is observed. Take some powdered sample and add dilute hydrochloric acid. No effervescence is observed.
c) Talc test	Take 5-10 mL of Solution A, add small amount of ammonium carbonate solution and boil. No white precipitate is observed.

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5.13 Porosity (HPI)

Put 1-2 drops of Dispensing alcohol to the center of the sphere (globule). Cut the globule with sharp blade into two halves. Check the two halves for absorption.

Impregnation of dispensing alcohol to the center of the sphere should not more than 50 seconds. (Note: The globule should not dissolve in dispensing alcohol)

5.14 Uniformity of impregnation (As per EP/BP)

None of the individual values deviate by more than 10% from the average of 10 determinations. Determine the uniformity of impregnation using either method A or method B. Carryout 10 individual determinations.

Method A	**Methylene blue impregnation solution:** Use a freshly prepared solution. Dissolve 1.0 g of methylene blue R in 50 mL of ethanol (70 percent v/v) R and dilute to 1000.0 mL with the same solvent. **Impregnation:** Impregnate a suitable quantity of pillules for homoeopathic preparations with a suitable quantity of the methylene blue impregnation solution to achieve a content of 10µL of impregnation solution per gram of pillules. **Test solution:** Dissolve 5.00 g of the impregnated pillules in Water and dilute to 25.0 mL with the same solvent. **Reference solution:** Dilute 1.0 mL of the methylene blue impregnation solution to 100.0 mL with water. To 5.0 mL of this solution add 5.00 g of pillules for homoeopathic preparations, dissolve in water R and dilute to 25.0 mL with the same solvent. Measure the absorbance of the test solution and the reference solution at 665nm. Calculate the percentage of impregnation of the pillules for homoeopathic preparations using the following expression: $\frac{A_1 \times 500}{A_2 \times 500}$ A_l: Absorbance of the test solution; A_2: Absorbance of the reference solution; m: Mass of the impregnated pillules used to prepare the test solution, in grams.
Method B	**Caffeine Method:** As the test results are particularly influenced by the procedures for impregnation and drying of the pillules, the parameters of these procedures are defined and stated with the result. Caffeine impregnation solution: Prepare a 15 g/L solution of caffeine R in ethanol (70% v/v) **Impregnation:** Impregnate a suitable quantity of pillules for homoeopathic preparations with a suitable quantity of the caffeine impregnation solution to achieve a content of 10µL of impregnation solution per gram of pillules. During the preparation of the following solutions, if the Pillules are not fully dissolved, sonicate the dispersion for 30 min and cool to 20°C. Before measuring

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	the absorbance, centrifuge the dispersion and filter the supernatant through a membrane filter (nominal pore size 0.45 µm). **Test solution:** To 5.00 g of the impregnated pillules add 30 mL of water R. Shake manually then sonicate until complete dissolution of the pillules. Dilute to 50.0 mL with water. **Reference solution:** Dilute 1.0 mL of the caffeine impregnation solution to 100.0 mL with water. To 5.0 mL of this solution add 5.00 g of pillules for homoeopathic preparations and 30 mL of water R. Shake manually then sonicate until complete dissolution of the pillules. Dilute to 50.0 mL with water. **Compensation liquid:** To 5.00 g of pillules for homoeopathic preparations add 30 mL of water. Shake manually then sonicate until complete dissolution of the pillules. Dilute to 50.0 mL with water. **Measure the absorbance** of the test solution and the reference solution at 273 nm by comparison with the compensation liquid. Calculate the percentage of impregnation of the pillules for homoeopathic preparations using the following expression: $\frac{A_1 \times 500}{A_2 \times m}$ A_1: Absorbance of the test solution; A_2: Absorbance of the reference solution; m: Mass of the impregnated pillules used to prepare the test solution, in grams.

5.15 Microbial contamination:

Should have values as per the method prescribed in USP 1111: Microbiological Examination of Non-sterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use.

As per EP/BP:

TAMC: Acceptance criterion 102 CFU/g
TYMC: acceptance criterion 101 CFU/g
Absence of Staphylococcus aureus
Absence of Pseudomonas aeruginosa

6. Shelf Life

A shelf Life of 3 years is recommended, subject to data as per in-house stability studies.

7. Packing and Marking

7.1 Packing

The material shall be packed in clean, sound and dry container made of metal, glass, and food grade polymers. The container shall be free from any fungal or insect infestation and should not impart any foreign smell. Each container shall be securely closed and sealed. They can also be packed in airtight plastic bags in secondary packaging of Cartons as per IS 10146: Polyethylene for its Safe Use in Contact with Foodstuffs, Pharmaceuticals and Drinking Water.

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7.2 Marking

The packaging shall be securely closed and marked with the following particulars, legibly and indelibly:

a) Size of globules
b) Name and address of the manufacturer or packer including contact details;
c) Name of the material;
d) Net quantity;
e) Date of Manufacturing;
f) Date of packing;
g) Best before date;
h) Batch or code number;
i) QR Code for Authentication (Optional);
j) Trade-name or brand name, if any; and
k) Any other markings required under the *Legal Metrology (Packaged Commodities) Rules, 2011, and the Food Safety and Standards (Packaging and Labelling) Regulation, 2011* or its latest version as applicable.

7.3 BIS Certification Marking

The product(s) conforming to the requirements of this standard may be certified as per the conformity assessment schemes under the provisions of the Bureau of Indian Standards Act, 2016 and the Rules and Regulations framed thereunder, and the products may be marked with the Standard Mark.

8. Sampling

Representative samples of the material shall be drawn, and tested for conformity to this specification as prescribed in IS 6287.

9. Quality of Reagents

Unless specified otherwise, Analytical grade reagents and distilled water (see IS 1070) shall be used in tests.

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