Powdered Digitalis

Digitalis Pulverata

ジギタリス末

Powdered Digitalis is the powder of Digitalis, or an admixture with sufficient starch or Lactose. It contains not less than 8 and not more than 13 Digitalis Units in 1 g.

Description Powdered Digitalis occurs as a green to grayish green powder. It has a slight odor, and an extremely bitter taste.

Under a microscope, Powdered Digitalis reveals multicellular hairs, glandular hairs, palisade tissues, sponge tissues, and thin vessels; the multicellular hairs of 2 to 8 cells, apex acute, mostly somewhat curved and some of them collapsed; small glandular hairs with a 1- or 2-celled stalk and a 1- or 2-celled head; no crystal of calcium oxalate in the tissues.

Identification To 1 g of Digitalis add 10 mL of diluted ethanol (7 in 10), boil for 2 minutes, and filter. To 5 mL of the filtrate add 10 mL of water and 0.5 mL of lead subacetate TS, shake, and filter. To the filtrate add 5 mL of chloroform, shake, and separate the chloroform layer. Evaporate the chloroform gently on a water bath. Cool, add 1 mL of a solution of iron (III) chloride hexahydrate in acetic acid (100) (1 in 10000) to the residue, shake well, and underlay gently with 1 mL of sulfuric acid: at the zone of contact of the two liquids a red-brown ring is produced, and the upper layer near the zone of contact gradually changes to dark green, and finally to a dark color.

Loss on drying Not more than 5.0%.

Total ash Not more than 12.0%.

Acid-insoluble ash Not more than 5.0%.

Assay (i) Animals—Select healthy adult pigeons, the heaviest of which weighs less than twice the mass of the lightest. Divide the selected pigeons into two groups, each consisting of more than six pigeons which are as nearly alike as practicable with respect to sex and mass, so that average mass of the group receiving the standard solution does not differ by more than 30% from the average mass of the group receiving the sample solution. Withhold food but allow water for 16 to 28 hours prior to the test.

(ii) Standard stock solution—Transfer about 1 g of Digitalis Reference Standard, accurately weighed, to a glass-stoppered, 50-mL hard-glass bottle, and add 10 mL of diluted ethanol (4 in 5) per 1 g of the standard. Insert the stopper, the upper one-third of which is greased lightly with petrolatum. Shake the mixture between 20°C and 30°C for 24 hours by mechanical means which continuously brings the solid material into fresh contact with the liquid phase. Promptly centrifuge the mixture, decant the supernatant liquid into a suitable container, and use this solution as the standard stock solution. Preserve this solution between 1°C and 10°C before use, and use within 30 days.

(iii) Standard solution—On the day of the assay, dilute a portion of the standard stock solution with isotonic sodium chloride solution so that the estimated fatal dose per kg of body mass of the ani2mals will be about 15 mL.

(iv) Sample stock solution—Transfer about 1 g of Digitalis, reduced to a fine powder and accurately weighed, to a glass-stoppered, 50-mL hard-glass bottle, and proceed as directed in the standard stock solution. Use this solution as the sample stock solution. Preserve this solution between 1°C and 10°C before use, and use within 30 days.

(v) Sample solution—On the day of the assay, dilute a portion of the sample stock solution with isotonic sodium chloride solution so that the estimated fatal dose per kg of body mass of the animals will be about 15 mL.

(vi) Procedure—Fix the animals, and, if necessary, lightly anesthetize with diethyl ether. Expose an alar vein, and cannulate with a suitable cannula, previously filled with isotonic sodium chloride solution. Place the standard solution and the sample solution in a burette calibrated to 0.05 mL, and connect it with the cannula using a vinyl tube. Inject the standard solution and the sample solution from the burette after ensuring the absence of air bubbles in the burette, vinyl tubes and cannula, or inject them using an injection syringe calibrated to 0.01 mL through the cannula. The injection volume of the standard solution and the sample solution is equivalent to 1 mL per kg of body mass of the animals, and the duration of the injection is 2 to 3 seconds. Repeat this dose at 5-minute intervals thereafter until the animals die of cardiac arrest. If the average number of doses for any given solution required to produce death is less than 13 or more than 19, or if the larger average exceeds the smaller in the same assay by more than 4 doses, regard these data as preliminary. Use them as a guide, and repeat with a fresh, higher or lower dilution.

(vii) Calculation—Designate the number of animals in the groups injected with the standard solution and the sample solution as N_S and N_T, respectively. Designate the total number of doses required to produce death in each group as Y_S and Y_T, respectively, and designate their average values as $\overline{Y}_S$ and $\overline{Y}_T$, respectively.

$$\text{Units in each of Powdered Digitalis} = \frac{\text{units in each mL of the standard solution}}{\text{mass (g) of Powdered Digitalis in each mL of the sample solution}} \times \frac{\overline{Y}_S}{\overline{Y}_T}$$

Compute L (P = 0.95) by using following equation: L should be not more than 0.30. If it exceeds 0.30, repeat the assay by increasing the number of animals or improving the assay conditions, until L becomes not more than 0.30.

$$L = 2\sqrt{(C-1)\left[C \times \left(\frac{\overline{Y}_S}{\overline{Y}_T}\right)^2 + \frac{N_T}{N_S}\right]}$$

$$C = \frac{\overline{Y}_T^2}{\overline{Y}_T^2 - \frac{s^2 t^2}{N_T}}$$

$$s^2 = \frac{\Sigma y^2 - \frac{Y_S^2}{N_S} - \frac{Y_T^2}{N_T}}{n}$$

Σy^2: The sum of values which are obtained by squaring separately the number of the injection for the standard solution and the sample solution.

$n = N_S + N_T - 2$

t^2: Value shown in the following table against n for which s^2 is calculated.

n	$t^2 = F_1$	n	$t^2 = F_1$	n	$t^2 = F_1$
1	161.45	13	4.667	25	4.242
2	18.51	14	4.600	26	4.225
3	10.129	15	4.543	27	4.210
4	7.709	16	4.494	28	4.196
5	6.608	17	4.451	29	4.183
6	5.987	18	4.414	30	4.171
7	5.591	19	4.381	40	4.085
8	5.318	20	4.351	60	4.001
9	5.117	21	4.325	120	3.920
10	4.965	22	4.301	∞	3.841
11	4.844	23	4.279		
12	4.747	24	4.260		

Containers and storage Containers—Tight containers. Storage—Light-resistant.

Dioscorea Rhizome

Dioscoreae Rhizoma

サンヤク

Dioscorea Rhizome is the rhizome (rhizophore) of *Dioscorea japonica* Thunberg or *Dioscorea batatas* Decaisne (*Dioscoreaceae*), from which the periderm has been removed.

Description Cylindrical or irregular cylindrical rhizome, 5 - 15 cm in length, 1 - 4 cm in diameter, occasionally longitudinally split or transversely cut; externally whitish to yellowish white; fractured surface, whitish, smooth and powdery; hard in texture but breakable. Practically odorless and tasteless.

Identification **(1)** To the cut surface of Dioscorea Rhizome add dilute iodine TS dropwise: a dark blue color develops.

(2) To 0.2 g of pulverized Dioscorea Rhizome add 2 mL of acetic anhydride, warm on a water bath for 2 minutes, and filter. To 1 mL of the filtrate add 0.5 mL of sulfuric acid carefully to make two layers: a red-brown to purple-brown color appears at the zone of contact.

Loss on drying Not more than 14.0% (6 hours).

Total ash Not more than 6.0%.

Acid-insoluble ash Not more than 0.5%.

Powdered Dioscorea Rhizome

Dioscoreae Rhizoma Pulveratum

サンヤク末

Powdered Dioscorea Rhizome is the powder of Dioscorea Rhizome.

Description Powdered Dioscorea Rhizome occurs as nearly yellowish white to white; odorless and tasteless.

Under a microscope, Dioscorea rhizome powder reveals starch grains; fragments of parenchyma cells containing starch grains; raphides of calcium oxalate, 100 to 200 μm in length and its containing mucilage cells; ring and scalariform vessels, 15 to 35 μm in diameter; starch grain isosceles deltoid or oblong, solitary, 18 to 35 μm, hilum and striation being distinct.

Identification To 0.2 g of Powdered Dioscorea Rhizome add 2 mL of acetic anhydride, warm on a water bath for 2 to 3 minutes, and filter. To the filtrate add 0.5 mL of acetic anhydride, shake, and add carefully 0.5 mL of sulfuric acid to make two layers: a red-brown to purple-brown color develops at the zone of contact.

Loss on drying Not more than 14.0% (6 hours).

Total ash Not more than 6.0%.

Acid-insoluble ash Not more than 0.5%.

Containers and storage Containers—Tight containers.

Diphenhydramine and Bromovalerylurea Powder

ジフェンヒドラミン・ワレリル尿素散

Method of preparation

Diphenhydramine Tannate	90 g
Bromovalerylurea	500 g
Starch, Lactose, or their mixture	a sufficient quantity
To make	1000 g

Prepare as directed under Powders, with the above ingredients.

Description Diphenhydramine and Bromovalerylurea Powder occurs as a slightly grayish white powder.

Identification **(1)** To 0.1 g of Diphenhydramine and Bromovalerylurea Powder add 5 mL of dilute hydrochloric acid, 1 mL of ethanol (95) and 10 mL of water, shake, and filter. To the filtrate add 10 mL of sodium hydroxide TS, and extract with 10 mL of chloroform. Separate the chloroform layer, add 1 mL of bromophenol blue TS, and shake: a yellow color develops in the chloroform layer (diphenhydramine tannate).

(2) Shake 0.02 g of Diphenhydramine and Bromovalerylurea Powder with 10 mL of diethyl ether, filter, and evaporate the filtrate on a water bath. Dissolve the residue in 2 mL of sodium hydroxide TS, and add 5 mL of dimethylglyoxime-thiosemicarbazide TS, and heat on a water bath for 30 minutes: a red color develops (bromovalerylurea).

(3) Shake 0.3 g of Diphenhydramine and Bromovalerylurea with 5 mL of methanol, filter, and use the filtrate as the sample solution. Dissolve 0.15 of bromovalerylurea and 0.03 g of diphenhydramine tannate in 5 mL each of methanol, and use the solutions as standard solution (1) and standard solution (2). Perform the test as directed under the Thin-layer Chromatography with these solutions. Spot 5 μL each of the sample solution and the stan-