

3. Even though preservatives are not added in ampoules, ascorbic acid injection contains preservative. Why?
4. How is ascorbic acid injection sterilized?
5. Show the calculations required for the manufacture of 60 ltr of ascorbic acid injection.
6. Describe the method of filling of drug solution into ampoules.
7. Explain the methods of sealing of ampoules.
8. Enumerate the problems associated with sealing of ampoules. Explain them giving possible solutions.
9. Draw the figure showing proper and improper seals of ampoules.

Calcium Gluconate Injection IP

Experiment No. 13

Date:

Aim : To prepare and submit 2 ampoules, each containing 10 ml of calcium gluconate injection IP.

Formula : As per IP

Ingredients	Official formula	Working formula
Calcium gluconate	9.65 g	
Calcium D-saccharate	0.35 g	
Water for injection	q.s.	100 ml

Manufacturer's Definition (IP) : Calcium gluconate injection is a sterile solution of calcium gluconate in water for injection. Not more than 5.0% of the calcium gluconate may be replaced with a suitable calcium salt as a stabilising agent.

Standards (IP) : Calcium gluconate injection contains a quantity of calcium equivalent to not less than 8.5 per cent and not more than 9.4 per cent of the stated amount of calcium gluconate, $C_{12}H_{22}O_{14} \cdot Ca \cdot H_2O$.

Usual Strengths : The equivalent of 500 mg of calcium gluconate in 5 ml; the equivalent of 1 g of calcium gluconate in 10 ml (A 10% w/v solution of calcium gluconate contains approximately 0.45 mmol of Ca^{++} per ml).

Ten per cent w/v solution of calcium gluconate is also available in 10, 50, and 100 ml vials.

Type : Monophasic liquid dosage form—solution.

Theory

Calcium gluconate is slowly soluble in about 30 parts of water and soluble in about 5 parts of boiling water. Calcium in the form of calcium gluconate is used in the strength of 10% w/v. In fact 10% solution of calcium gluconate in water gives a saturated solution. Any temperature

fluctuations during storage yield crystallization of calcium gluconate. Therefore, IP prescribes to replace a part of calcium gluconate (not more than 5% of the total) by an equal amount of more soluble calcium salt, such as calcium D-saccharate or calcium lactobionate. These soluble calcium salts are called stabilizing agents. The pH of the calcium gluconate injection can be adjusted from 6.0 to 8.2 using sodium hydroxide and/or hydrochloric acid solutions. It is prepared in a single dose container, preferably Type I glass container.

Calcium gluconate is usually administered intravenously as a 10% solution, slowly by direct intravenous injection, or by continuous or intermittent intravenous injection. Maximum administration rates of 1.5 and 2 ml/min have been recommended for direct intravenous injection. By intermittent infusion a maximum of 200 mg/min has been suggested. Calcium gluconate has been given by intramuscular or, rarely, subcutaneous injection to adults, but these routes are not recommended because of possible tissue necrosis, sloughing, and abscess formation.

Calcium gluconate is compatible with substances such as dextrose 5%, sodium chloride 0.9% aminophylline, amphotericin B, ascorbic acid injection, chloramphenicol sodium succinate, furosemide, heparin sodium, and penicillin G sodium. Calcium gluconate is incompatible with substance such as metoclopramide HCl, indomethacin sodium trihydrate, citrates, soluble carbonates, phosphates, and sulfates.

Apparatus and Chemicals

Ampoules, 10 ml	2	Calcium gluconate
Beaker, 250 ml	1	Calcium D-saccharate
Beaker, 100 ml	1	Water for injection
Measuring cylinder, 10 ml	1	
Syringe with needle, 10 ml	1	
G-4 filter	1	
Autoclave	1	

Procedure

Depending on the number of injections to be submitted, the working formula is calculated. The manufacturing operations are done in clean rooms.

Cleaning of ampoules : Cleaning of Type I glass ampoules is carried out by following the usual procedure.

Preparation of calcium gluconate solution

1. The desired amount of calcium gluconate and calcium D-saccharate are accurately weighed.

2. On account of solubility problems, calcium gluconate is first dissolved in water for injection in beaker with the aid of heat.
3. Then calcium D-saccharate is dissolved in the above solution.
4. The solution is allowed to cool.
5. After cooling, the drug solution is filtered through G-4 filter (or Whatmann filter paper) to remove any foreign particles.

Filling into ampoules : Filling of ampoules (Type I) is done following the usual procedure.

Sealing of ampoules : The ampoules can be sealed by using pull-sealing technique.

Sterilization : In general, calcium gluconate injection is subjected to terminal sterilization. This can be achieved by autoclaving at 121°C at 15 lbs/inch² for 30 minutes.

Packing : Ampoules are packed in a suitable ampoule box and labeled.

Composition : Each ml contains 100 mg of total calcium.

Category : Calcium replenisher (Calcium gluconate injection is supplemented where dietary calcium intake is deficient and in impaired absorption, due to old age and in case of osteoporosis. This injection is indicated in case of hypocalcaemic tetany and also in cardiac resuscitation).

Dose : 1 to 2 g (500 mg of calcium gluconate is approximately equivalent to 2.3 mmol of Ca⁺⁺).

Storage : Store in a cool place.

Auxiliary Labels : (1) Discard, if any particulate matter is present.

- (2) If crystallization has occurred during storage, warming may dissolve the precipitate. The injection must be clear at the time of use.

Route of Administration : Intramuscular or slow intravenous route.

Date of Expiry : 3 years from the date of manufacture.

Quality Control

1. Particulate matter : absent / present ✓
2. Leaking : no / yes ✓
3. Tip : sharp / round ✓
4. Charring : absent / present ✓