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UNIVERSITY OF RUHUNA - FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FOURTH BPHARM PART II EXAMINATION – SEPTEMBER 2023

PH 4223 QUALITY CONTROL – SEQ PAPER

TIME: TWO HOURS

INSTRUCTIONS

- Answer **all** questions in the booklet provided.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

1.

1.1. Qualification is an important concept in Good Manufacturing Practices (GMP) related to pharmaceuticals. Define the following terms. ***(20 marks)***

1.1.1. Design qualification (DQ)

1.1.2. Installation qualification (IQ)

1.1.3. Operational qualification (OQ)

1.1.4. Performance qualification (PQ)

1.2. Answer the following questions based on essential aspects of GMP related to pharmaceuticals.

1.2.1. Give two examples each for critical product defects and major product defects. ***(20 marks)***

1.2.2. Briefly describe the types of self-inspections conducted by pharmaceutical companies. ***(30 marks)***

1.3. Comment on the following statement "*Conducting only finish product quality control tests is sufficient to ensure the quality of medicines*". ***(30 marks)***

2.

2.1. Establishment of an efficient product recall procedure is important in pharmaceutical quality assurance. Justify the above statement. ***(30 marks)***

2.2. Answer below given questions using the provided monograph of Dopamine Intravenous Infusion.

2.2.1. State the name of the active pharmaceutical ingredient with upper and lower limits of the content. ***(20 marks)***

2.2.2. List the main tests that will appear in the finished product certificate of analysis (CoA) of Dopamine Intravenous Infusion. ***(20 marks)***

2.3. Quality control is more critical in sustained-action products than in immediate-release products. Briefly explain the reasons.

(*30 marks*)

3.

3.1.

3.1.1. Name two viscometers used to determine the viscosity of syrup dosage forms.

(*04 marks*)

3.1.2. Briefly describe the role of viscosity as a quality parameter of syrups. (*20 marks*)

3.2.

3.2.1. State two factors affecting the hardness of a tablet dosage form. (*10 marks*)

3.2.2. Elaborate how hardness would affect the disintegration and dissolution properties of a tablet dosage form.

(*10 marks*)

3.3.

3.3.1. In quality assessments, the disintegration test of a tablet dosage form is usually carried out prior to the dissolution test. Explain the reasons. (*20 marks*)

3.3.2. Describe the steps of evaluating *in-vitro* dissolution of solid dosage forms.

(*36 marks*)

4.

4.1.

4.1.1. Define the term pharmaceutical packaging. (*10 marks*)

4.1.2. Briefly describe three functions of packaging materials. (*25 marks*)

4.1.3. List four types of glasses that are used for pharmaceutical packaging. (*10 marks*)

4.1.4. Write two quality control tests used to determine the chemical resistance of glass containers.

(*10 marks*)

4.1.5. Briefly describe the bubble test which is used to test the packaging integrity of glass containers.

(*25 marks*)

4.2.

4.2.1. Define the term "liquefaction time". (*10 marks*)

4.2.2. Mention two methods used to determine the liquefaction time of suppositories.

(*10 marks*)

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Dopamine Infusion

Dopamine Intravenous Infusion

Action and use

Dopamine receptor antagonist; beta$_1$-adrenoceptor agonist; alpha-adrenoceptor agonist.

DEFINITION

Dopamine Infusion is a sterile solution containing Dopamine Hydrochloride. It is supplied as a ready-to-use solution or it is prepared by diluting either Sterile Dopamine Concentrate or Dopamine Hydrochloride for Injection with a suitable diluent in accordance with the manufacturer's instructions.

The infusion complies with the requirements stated under Parenteral Preparations and with the following requirements.

When supplied as a ready-to-use solution, the intravenous infusion complies with the following requirements.

Content of dopamine hydrochloride, $C_8H_{11}NO_2,HCl$
95.0 to 105.0% of the stated amount.

Content of glucose, $C_6H_{12}O_6$
4.75 to 5.25% w/v.

CHARACTERISTICS

A colourless liquid.

IDENTIFICATION

A. Saturate a volume containing 0.1 g of Dopamine Hydrochloride with *sodium chloride* and extract with three 20-mL quantities of *butan-1-ol*. Filter the combined extracts through *anhydrous sodium sulfate* and evaporate the filtrate to dryness. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of dopamine hydrochloride *(RS 113)*.

B. To a volume containing 10 mg of Dopamine Hydrochloride add 0.1 mL of *iron(III) chloride solution R1*. An intense green colour is produced.

TESTS

Acidity

pH, 3.0 to 4.5, Appendix V L.

5-Hydroxymethylfurfural

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Use the intravenous infusion.

(2) 0.0025% w/v of *5-hydroxymethylfurfural* in *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 2 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 284 nm.

(f) Inject 20 µL of each solution.

MOBILE PHASE

0.05M *disodium hydrogen orthophosphate* adjusted to pH 7.0 with *orthophosphoric acid*.

LIMITS

In the chromatogram obtained with solution (1), the area of any peak corresponding to 5-hydroxymethylfurfural is not greater than the area of the principal peak in the chromatogram obtained with solution (2) (0.05%, determined with reference to the content of glucose).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute the infusion with sufficient mobile phase to produce a solution expected to contain 0.032% w/v of Dopamine Hydrochloride.

(2) Dilute 1 volume of solution (1) to 50 volumes with the mobile phase.

(3) Dilute 1 volume of solution (1) and 1 volume of a solution containing 0.030% w/v each of *4-ethylcatechol* and *3,4-dimethoxyphenethylamine* to 50 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Assay may be used.

Under the prescribed conditions, the retention time of dopamine is about 5 minutes, of 4-ethylcatechol about 3 minutes and of 3,4-dimethoxyphenethylamine, about 12 minutes.

LIMITS

In the chromatogram obtained with solution (1):

the area of any *secondary peak* is not greater than 1.25 times the area of the principal peak in the chromatogram obtained with solution (2) (2.5%);

not more than one such peak has an area greater than the area of the principal peak in the chromatogram obtained with solution (2) (2%).

Bacterial endotoxins

Carry out the *test for bacterial endotoxins*, Appendix XIV C. Dilute the intravenous infusion, if necessary, with *water BET* to give a solution containing 1.6 mg of Dopamine Hydrochloride per mL (solution A). The endotoxin limit concentration of solution A is 26.67 IU per mL.

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

(1) Dilute a suitable volume of the infusion with mobile phase to produce a solution expected to contain 0.0032% w/v of Dopamine Hydrochloride.

(2) 0.0032% w/v of *dopamine hydrochloride BPCRS* in the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *end-capped octadecylsilyl silica gel for chromatography* (5 µm) (Nucleosil C18 is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 2 mL per minute.

(d) Use an ambient column temperature.

(e) Use a detection wavelength of 280 nm.

(f) Inject 20 µL of each solution.

MOBILE PHASE

2 volumes of 0.1M *disodium edetate*, 10 volumes of *glacial acetic acid*, 300 volumes of *acetonitrile* and 700 volumes of 0.005M *sodium dodecyl sulfate*.

DETERMINATION OF CONTENT

Calculate the content of $C_8H_{11}NO_2,HCl$ in the infusion using the declared content of $C_8H_{11}NO_2,HCl$ in *dopamine hydrochloride BPCRS*.