19.2.03

AOAC Official Method 974.40 Guaifenesin in Drugs Polarographic Method First Action 1974 Final Action 1974

(Not applicable in presence of salicylate.)

A. Apparatus

(a) *Polarograph.*—Any voltammetric or polarographic instrument with necessary accessories (cells, electrodes, Hg, capillaries) capable of scanning up to 3.0 V in either positive or negative direction.

(b) *Micro or standard cell, H-shaped.*—Saturated calomel electrode, with 3% KCl-agar plug.

(c) Water bath.—Maintain at $65 \pm 1^{\circ}$ C in freely circulating H₂O bath.

B. Reagents

(a) Potassium nitrate solution.—1M. Weigh 50.5 g KNO₃ into 500 mL volumetric flask, dilute to volume with H_2O , and mix.

(b) Dilute sulfuric acid solution.—10% (v/v). Dilute 20 mL H_2SO_4 (1 + 1) to 100 mL with H_2O and mix.

(c) Gelatin maximum suppressor.—1 mg/mL. Accurately weigh 100 mg gelatin into 100 mL volumetric flask, and dissolve in small amount H_2O on steam bath. Cool, dilute to volume with H_2O , and mix. Prepare fresh daily, as needed.

(d) Supporting electrolyte.—pH 10.4. Weigh 53.5 g NH_4Cl into 1 L volumetric flask, add 400 mL NH_4OH , mix to dissolve, and dilute to volume with H_2O .

(e) Guaifenesin standard solution.—1 mg/mL. Accurately weigh 25 mg USP guaifenesin Reference Standard into 25 mL volumetric flask. Dilute to volume with H_2O and mix.

C. Preparation of Test Portion

(a) Syrups.—Quantitatively transfer accurately measured test portion containing ca 100 mg guaifenesin to 125 mL separator, add 10 mL dilute H_2SO_4 , and extract with four 20 mL portions CHCl₃, and then with 15 mL CHCl₃. Collect CHCl₃ extracts in second separator and wash with 10 mL H_2O . Filter CHCl₃ layer through pledget of CHCl₃-washed cotton into 100 mL volumetric flask. Rinse separator with 2–3 mL CHCl₃ and add wash to volumetric flask. Dilute to volume with CHCl₃ and mix.

(b) *Tablets.*—Determine average weight/tablet. Grind without loss to pass No. 60 sieve. Accurately weigh powder containing ca 50 mg guaifenesin and transfer to 125 mL separator. Add 10 mL H₂O

and shake 2 min. Proceed as in (**a**), beginning "...add 10 mL dilute H_2SO_4 ,...".

D. Derivative Formation

Pipet duplicate 10 mL aliquots for syrups or 20 mL aliquots for tablets of prepared test solution into separate 100 mL volumetric flasks and carefully evaporate to dryness with aid of air only. Add 10 mL H_2O to each and shake to dissolve guaifenesin. Label flasks as test portion and blank. Pipet 10 mL guaifenesin standard solution into third 100 mL volumetric flask and label as standard.

Pipet 3 mL H_2SO_4 (1 + 1) into each flask. Pipet 3 mL 1M KNO₃ into standard and test sample flasks and 3.0 mL H_2O into blank flask. Place flasks in 65°C constant temperature bath. When solutions reach 65°C, heat additional 60 min. Remove from bath and cool to room temperature. Into each flask pipet 25 mL electrolyte solution and 5 mL gelatin solution, cool to room temperature, dilute to volume with H_2O , and mix thoroughly.

E. Polarography

Transfer solution to polarographic cell and bubble N₂ through for 5 min with micro H cell or 10 min with standard H cell at moderate rate. Polarograph from -0.2 to -0.9 V against saturated calomel reference electrode. Measure height of diffusion current (I_d) at half-wave potential as follows: Draw line tangent to top of residual current extending to half-wave potential point. Draw line along top of limiting current extending to half-wave potential point. Measure vertical drop at half-wave potential between the 2 lines in convenient units.

Determine guaifenesin concentration by comparing wave height of test sample solution with those of standard and blank solutions.

Subtract diffusion current (I_d^b) of blank, if any, from test sample only. Perform all determinations at same current sensitivity and within same time span.

F. Calculations

(a) Syrup.—

mg Guaifenesin/mL = $100 \times (I_d - I_d^b) \times C/(I_d' \times V)$

(b) Tablets.—

mg Guaifenesin/tablet = $50 \times (I_d - I_d^b) \times C \times W_t / (I_d' \times W_s)$

where I_d , I_d^b , and I_d' = diffusion current of test sample, blank, and standard solutions, respectively; C = mg guaifenesin/mL standard solution; W_t and W_s = average tablet weight and weight test portion taken, respectively; and V = mL liquid preparation taken.

Reference: JAOAC 57, 756(1974).

CAS-93-14-1 (guaifenesin)