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NOTE

Manufacturing of Tinidazole by Recovering and Recycling Catalyst

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In this paper, the recycle process of tungstic acid by recovering it from waste during the manufacture of tinidazole is described. The recovered tungstic acid gives desired quality and quantity of tinidazole.

Key Words: Recovery, Tinidazole, Tungstic acid.

Tinidazole is well-known antimicrobial drugs as well as sensitizers of hypoxic tumors in conjunction with radiotherapy and 1-(2-ethyl-sulfonyl-ethyl)-2-methyl-5-nitroimidazole particularly, is known to be useful for the treatment of amebiasis while other derivatives[1,2]. The conventional manufacturing process of tinidazole involves first, a condensation step in the presence of sulfuric and acetic acids to give an intermediate, 1-(2-ethyl-thio-ethyl)-2-methyl-5-nitro-imidazole which in the second step undergoes oxidation with H_2O_2 in presence of tungstic acid. Like several other processes practiced in pharma industry, the above process also results in the production of large amount of wastes due to (i) use of stoichiometric quantities of both acetic and sulfuric acids and hence the work up as well as recovery of the intermediate becomes tedious (ii) use of ammonium molybdate or tungstic acid in the oxidation step, which gets converted to ammonium tungstate due to addition of liquor ammonia for work up of the reaction[3,4]. The present work described the catalyst can be recover and recycle in the manufacturing of tinidazole economically and environmental friendly. No literature found on for recovery process of tungstic acid.

Technical grade tungstic acid is made available for comparative study. The used tungstic acid was dissolved in nitric acid and pH was adjusted at 1. The precipitated tungstic acid filtered through Whatmann paper No. 41 and was dried in oven for further process (Yield 50 %).

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Preparation of tinidazole: 2-Methyl-5-nitro-imidazole (800 g) was taken in a round bottom flask fitted with a reflux condenser and stirring arrangement. To this 200 mL of acetic acid was added along with 300 mL 98 % sulfuric acid and this mixture was kept under stirring for 9 h at 80-85 ºC with the addition of 440 g 2-ethyl-thio-ethanol. The unreacted 2-methyl-5-nitro-imidazole was precipitated by adjusting the pH to 3 by adding 24 % liquid ammonia solution and isolated by filtration. Filtrate obtained was a mixture of aqueous solution of salts and organic layer, which contains intermediate product. The aqueous layer was discarded and organic layer was extracted using 15 % HCl. The intermediate product 1-(2-ethyl-thio-ethyl)-2-methyl-5-nitroimidazole was separated as a hydrochloride in aqueous solution from organic layer and oxidized using stoichiometric quantities of 50 % H_2O_2 and tungstic acid (8 g) as catalyst at 50-55 ºC. During work up, 25 % aqueous ammonia was added to precipitate tinidazole, which was isolated by filtration while tungstic acid was converted to ammonium tungstate which goes in filtrate.

To standardize the process, the quantity of caustic soda was also added with conc. nitric acid. The stiocometrically suitable quantities were decided based on desired quality and quantity. The recovered catalyst was tested for its purity by previously validated analytical method and found suitable for indented use.

Table-1 shows that tungstic acid can be recovered successfully for recycle for its further use.

TABLE-1
RECOVERY (%) OF TUNGSTIC ACID USING CAUSTIC SODA

Recovered tungstic acid (g)	Nitric acid (g)	Caustic soda	Yield (g)	Overall yield (%)
200	1000	32	102	51.0
200	1000	35	103	51.5
200	1000	34	101	50.5

Experiments are carried out with recovered catalyst and results are compared with the fresh catalyst (Table-2).

TABLE-2
COMPARISON DATA OF TINIDAZOLE YIELD BY FRESH AND RECOVERED CATALYST

Wt. catalyst (g)	Wt. 2MNI (g)	Recovered 2MNI (g)	Expected tinidazole (g)	Actual tinidazole (g)	Yield (%)
8	800	403	560	558	99
8	800	400	560	562	100
8	800	405	560	556	98
8	800	406	560	563	101

2MNI = 2-Methyl-5-nitro-imidazole.

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