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Research Paper Engineering

Cleaner Production process for manufacturing of Paracetamol - A case study

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ABSTRACT

Paracetamol is produced from p-nitrophenol, using iron-acid for hydrogenation. As a result, huge amount of hazardous waste is generated with high organic impurities and difficult to dispose of. Since, the scale of operation is very small and it will be very difficult for them to dispose even in common hazardous waste disposal sites, it will be worthwhile to employ catalytic hydrogenation or any other cleaner technology options so that the effluents/emissions/hazardous waste generation can be eliminated.

Key Words:

1.0 Introduction

Paracetamol is an important antipyretic and analgesic agent with weak anti-inflammatory effects. Paracetamol has been around as a drug for more than thirty years. Paracetamol, being a safe and low priced analgesic is quite popular worldwide. Medical opinion throughout the world is in favour of using paracetamol either by itself or in combination, over the established drug aspirin, due to its lower side effects. Paracetamol is being produced in India only by phenol and PNCB routes. Of these two routes, the PNCB route is more popular. The equipments are standardised. The end product conforms to IP specifications, and in the case of a few manufacturers even to BP/USP specifications. Many companies have claimed that their product assay is consistently above 98%. It is however, felt that some manufacturers do not have proper quality control checks. Their product quality may barely meet IP standards and may contain higher percentage of impurities.

2.0 Objective of Study work

Paracetamol is produced from p-nitrophenol, using iron-acid for hydrogenation. As a result, huge amount of hazardous waste is generated with high organic impurities and difficult to dispose of. Since, the scale of operation is very small and it will be very difficult for them to dispose even in common hazardous waste disposal sites, it will be worthwhile to employ catalytic hydrogenation or any other cleaner technology options so that the effluents/emissions/hazardous waste generation can be eliminated.

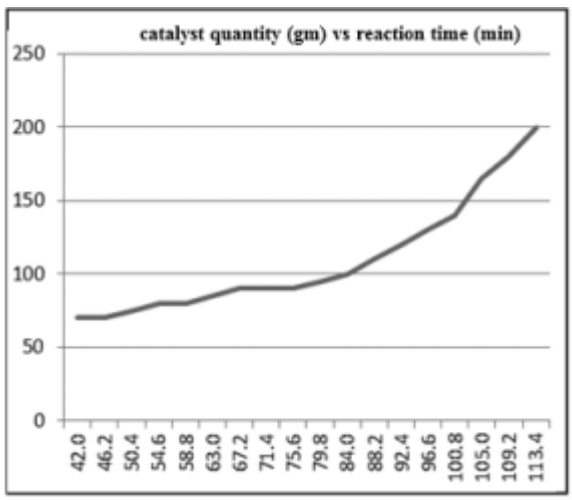
The objective of experimental work is to develop a cleaner production process for manufacturing of Paracetamol, with improvement in the efficiency of production, cost reduction and waste minimization.

Synthesis of p-aminophenol by catalytic hydrogenation of nitrobenzene discussed earlier suffers from three major disadvantages:

1. Formation of aniline as a side product;
2. Use of highly corrosive reagents like sulphuric acid; and
3. Difficulties in separation and purification of p-aminophenol from the reaction mass in pure form.

The catalytic hydrogenation of p-nitrophenol is an alternative route for the synthesis of p-aminophenol, which obviates the above-mentioned problems to some extent.

The starting material for this route, i.e. p-nitrophenol can be obtained either by hydrolysis of p-chloronitrobenzene or direct nitration of phenol. Conventionally, the reduction step is accomplished using iron-acid reducing agent. The major disadvantage of the conventional process is that it uses large amounts of iron and produces almost equivalent amount of Fe-FeO sludge, which poses serious waste disposal problems. The difficulties in the separation of pure p-aminophenol from the reaction mass containing Fe-FeO sludge is yet another drawback of the conventional process. A comprehensive literature review indicates that the transition metal catalyzed hydrogenation of p-nitrophenol can provide a cleaner route for the synthesis of p-aminophenol. In general, several group VIII metal catalysts such as Pt, Pd and Ni etc. Have been reported previously for the hydrogenation of p-nitrophenol. The rate of hydrogenation using these catalysts was first order with respect to hydrogen. The rate of hydrogenation was first order with respect to p-nitrophenol at lower catalyst concentration and zero order at higher catalyst loading. An empirical rate equation was also proposed to describe the hydrogenation rate behaviour.



2.1 Reaction :

2.2 Experimental setup

The hydrogenation experiments were carried out in a 20-litre capacity high-pressure slurry reactor (autoclave). The reactor was fitted with an internal cooling coil and impeller with four-

blade stirrer capable of operations up to 1500-rpm. The reactor was maintained at a constant temperature with the help of a PID (Proportional-Integra-Derivative) controller, which provided alternate heating and cooling. Temperature and pressure in the reactor was recorded using a digital display. The reactor was also equipped with relevant safety features like high temperature/pressure cut off and safety rupture disc. The results show that that when catalyst quantity increases reactions time also increases.

2.3 Materials

p-Nitrophenol, 5% Pd/C (palladium with carbon coating) catalyst, solvent (acetic acid), hydrogen & nitrogen gas.

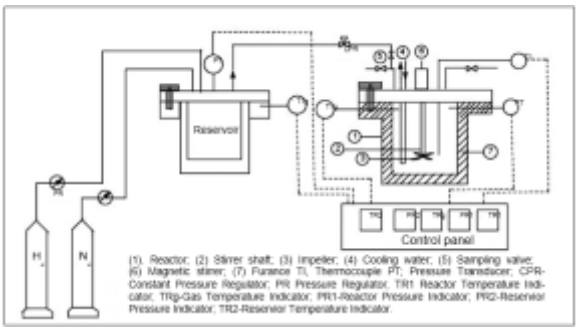


Figure 1: Schematic of the reactor set-up used for hydrogenation reactions

Pilot no	Catalyst quantity (gms)			Reaction time	p- amino phenol Conversion
	Fresh	Recycle	Total		
1	42	0	42	70	99.2
2	4.2	42	46.2	70	99.4
3	4.2	46.2	50.4	75	99.5
4	4.2	50.4	54.6	80	99.3
5	4.2	54.6	58.8	80	99.3
6	4.2	58.8	63	85	99.4
7	4.2	63	67.2	90	99.3
8	4.2	67.2	71.4	90	99.5
9	4.2	71.4	75.6	90	99.5
10	4.2	75.6	79.8	95	99.3
11	4.2	79.8	84	100	99.3
12	4.2	84	88.2	110	99.5
13	4.2	88.2	92.4	120	99.3
14	4.2	92.4	96.6	130	99.2
15	4.2	96.6	100.8	140	99.1
16	4.2	100.8	105	165	99.2
17	4.2	105	109.2	180	99.1
18	4.2	109.2	113.4	200	99.1

3.0 Conclusion

The most significant impact of the work presented in this project is the utility of the catalytic hydrogenation as the clean and environmentally acceptable route for the synthesis of p-aminophenol, an important intermediate for several drugs. Though, only a couple of examples are illustrated in this project , the impact of the present study is much wider since the catalytic hydrogenation of nitro compounds, in particular, have wide ranging applications in fine chemicals, pharmaceuticals as well as bulk commodity chemicals. This project has allowed better understanding of catalytic hydrogenation reaction systems, such as hydrogenation of p-nitrophenol to p-aminophenol. After verifying results, discussion and cost analysis of modified method, we conclude that the modified method is best – both qualitatively and economically. This will be extremely useful for design and scale-up of such systems.

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