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Integrated approach – Experimentation and Simulation approach to reduce the water consumption and effluent reduction in Pharmaceutical industry

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ABSTRACT
In Pharma Industry various reaction schemes are utilized for synthesis of the products. The reactions are Condensation, cyanization, esterification, Chlorination, Bromination and Reduction. In Specifically, to conduct the reduction reaction Hydrogen gas would be essential and it requires high pressure facility. Reduction reaction and high-pressure facility is key structure of all major and minor pharmaceutical industries. Hydrogen gas is having the key property of nonmetallic, odorless, tasteless, highly combustible diatomic gas and pyrophoric. To carryout, the Hydrogen pressure reaction which calls for the isolated condition and safety precaution consist of oxygen and Hydrogen sensors and vent designed with dump tank to release the hydrogen gas. As Hydrogen gas is Pyrophoric in nature and cannot be released into atmospheric directly which calls for the water dip tank for releasing the gas. As an engineering principle hydrogen gas will be dipped into the trap and diffusion will takes place and unabsorbed hydrogen will be released from Dump tank which consist of water . High volume of water is required for in the block and generating as effluent. It will be discharged into effluent treatment plant. The source point has identified as one of the effluent generation point and characteristic has done to understand the behavior. Experimental and Concept has created to recycle the water for utilizing the vessel cleaning purpose. Water is being used for the cleaning of the vessel and it has been optimized with the dyno chem to tool to reduce the water consumption in the study. This paper presents about the recycle of the water as part of source reduction and advance tool of dyno chem has been utilized to reduce and optimize the water consumption for the cleaning of the vessel in the hydrogenation block of pharmaceutical industry. The presentation of data gives the more evidence of variables and problem-solving approach for reduction of effluent at source.
Keywords **–** Dynochem, High pressure vessel, Wastewater reduction at source, Water recycle, Simulation approach.

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I. INTRODUCTION

1.1 Role of Hydrogenation Block in pharmaceutical industry: Various pressure vessels are installed in the serious of requirements which hydrogen gas is being used for the various reactions. It represented as hydrogenation blocks in pharmaceuticals industry. As part of process and procedure Inertization in the high-pressure vessel is essential. The performance as represented with apply of nitrogen with 1-3 Kg/cm^2 and repeat the procedure until oxygen has reduced below 4%. Water is being filled in the dump tank as key parameter before starting of the operation.

1.2 Batch Executional approach in pressure vessel:
High pressure process consists of the three key steps. Preparation of the key starting material catalyst charging and catalyst washing. Key starting material is being dissolved in the preparation vessel which will be transferred into pressure vessel. The second step involves the catalyst preparation and charging. Catalysis has been slurried in the separate vessel and it has been transferred into the pressure vessel. Third step consist of the catalyst washing. Additional quantity of solvent is being used in the catalyst vessel for complete removal of catalyst and finally slurry will be transferred to pressure vessel. After charging of the raw material, system should be free from the oxygen. To achieve the desired oxygen, the steps are being followed. Apply nitrogen gas into the Hydrogenator under stirring and build up the pressure to 1.0-3.0 kg/cm^2 at room temperature. Stir the reaction mixture for 5 – 10 minutes, release the nitrogen. Operation had been repeated for 3 to 4 times to achieve the oxygen content.

Oxygen content has been verified by monitoring system. Slowly apply hydrogen gas from hydrogen cylinder into the hydrogenator under stirring and build up the pressure to 2.0-3.0 kg/cm^2 and purge the hydrogen at 3.0-5.0 kg/cm^2 at desired temperature. Sample has been tested to check the key starting material content. After achieving the desired content of the key starting material, release the hydrogen gas into water seal trap and de-gas the reaction with Nitrogen gas for three times with 1-3 Kg/Cm^2 pressure each time. Reaction mixture filtered through pressure nutch filter.

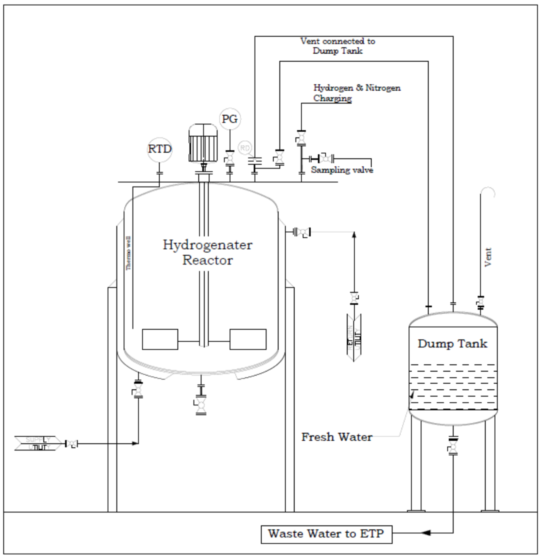


Fig. 1 Typical hydrogenation reactor set-up.

1.3 Point sources identification of effluent in high pressure block.

Hydrogenation procedure was executed as per the described summary in the above. It is being carried out in the high-pressure vessel. After completion of reaction, reaction mass will be filtered in the filtration setup for further processing. Water trap is the part of the high-pressure vessel. As part of the procedure, wastewater will be generated as effluent which will go for the effluent treatment plant.

The subsequent operation in the pressure vessel associated with cleaning for the entire system. The first step involves charging of the process solvent and rinse the system, which will be uploaded. The second step consist of charging of Methanol and water (1: 1 ratio) will be refluxed and after cooling the same will be unloaded. The third step will be charging of Methanol and rinse the system which will be unloaded. All the refereed cleaning procedure will be releasing the hazard waste and spent solvent.

1.4 Short summary of Dynochem:

Dynochem is simulation software which support for the process scale up and process design. This Paper presents to apply the new thought process for optimizing the water quantity by using the simulation tool of dyno chem.

1.5 Problem description:

High pressure vessel segment or block is required for all major pharmaceutical industry. It requires high amount of water for releasing the hydrogen gas through the trap and water to be replaced by batch to batch. The water generated as effluent which will be treated in the effluent treatment plant. Water is being used for the cleaning of the high-pressure vessel which will be released as spent solvent and mixer of water and solvent. It creates the environmental issues [1] and treatment is required to convert into pure solvent. More complicated solvent mixer will be sent for the incineration.

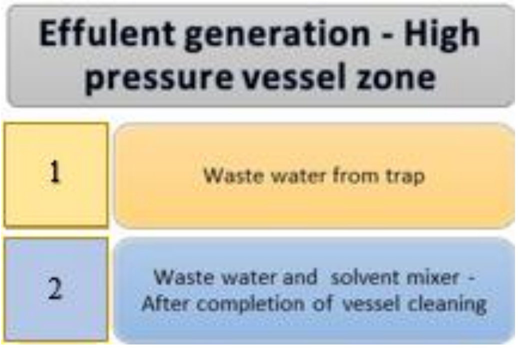


Fig. 2 Effluent generation high pressure vessel zone.

II. MATERIAL AND METHODS

2.1 Methods: The optimization of effluent and water reduction study were worked out with dynochem simulation software and creating experimental evidence for the treating the effluent

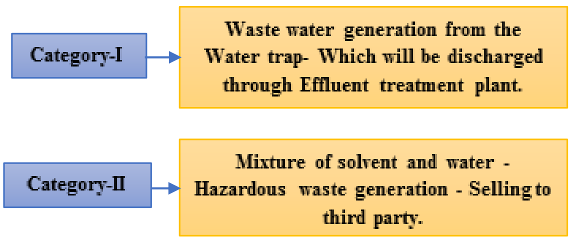
2.2 Material used: -

Wastewater from hydrogenation block, pH meter, TDS testing equipment, Micro filter and carbon.

2.3 Process and procedure for water recycle

Pharmaceutical batch process consist of the various reactions were carried out in the reactor with the pressure range of atmospheric. High pressure reactions were carried out in the pressure vessel due to compatibility nature and standard practices of industrial norms. Batch hydrogenation reactions were being carried out in the pressure vessel. The nature of the first effluent was being generated from the vent trap which connected with trap vessel. For Each batch, water needs to be replaced as fresh water and effluent was a part of generation. It would be treated in the effluent treatment plant [2]-[3]. The second part of effluent has been generated form the cleaning of the high-pressure vessel. It should be mandatory as part of the good manufacturing practices and quality standards of the products. The approach of cleaning calls for flushing of vessels with the process solvent and rinsed with water to remove primary residual content in the reactor. After primary rinsing of the reactor, mixer of water and methanol (1:1) blended and heated to remove undissolved solutes. The refluxed solvent mixture was sent to effluent treatment plant for furthered proceeding or selling of the solvent. Cleaning of the high-pressure vessel which generates the mixer of water and solvent effluent.

The two main sources of effluent generation from hydrogenation as described in below Fig .3



Category-I: Wastewater
Category-II: Water and methanol solvent

Fig.3 Effluent generation from hydrogenation block.

2.4 Wastewater characteristic:

Wastewater was being characterized as part of the work and results are tabulated. Characterization of the waste would the primary work for the creating the treatment methodology.

Waste Water characteristic			
Quality of Water	Value and source		
	1	2	3
pH	5.8	5.2	5.4
Conductivity: (µS/cm)	0.1	0.08	0.05
TDS (ppm)	520	564	590
COD	150	100	80
Color of waste	yellow	Slight yellow	No color
Particle	Observed no particle	Observed fine rust	Observed no particle

Table 1. Wastewater characteristics

2.5 Experimental procedure to recover water:

Wastewater was collected form the hydrogenation block. As per the characteristic, it consists of the slight color and particles. Effluent treatment has designed adequate sequence of steps [4] with the concept of primary filtration and secondary treatment with carbon which helps to remove the colour. To develop the concept and optimization, various micron filters was used to filer to remove the particles and ratified with the 0.45 filter paper. The second key issue observation would be slight color in one of the samples during characteristic. To remove the color, treatment technology has developed with the activated carbon treatment process [3]. Effluent was treated with the carbon and color was removed with the different experiments. Both optimizations of carbon and filtration process had clubbed and defined the structure of process. Based on the combination of the process, all particles and color were removed. The treatment process had been classified with primary and secondary which helps to get the pure quality of water and it can be recycled for cleaning of the vessel.

Lab experiment had made to define the process and configuration had been mapped.

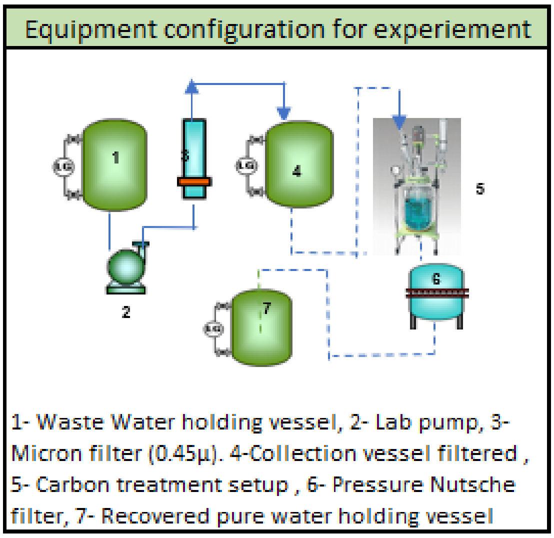


Fig.4 Proposed scheme recycling the trap water

III. EFFULENT OPTIMIZATION BY USING DYNOCHEM SIMULATION TOOL.

Pharmaceutical industries were majorly driven by various systems. In pharma, process were classified in to two steps. One is intermediate and second is API (Active pharmaceutical ingredient). Intermediate steps were being manufactured in non-clean room and final products were in clean room. Both steps calls for cleaning of the equipment as essential part of the practices. Batch process have been designed with the multipurpose products. Due to the product mix, cleaning was essential for the process industry. Based on the cleaning matrix, effluent will be generating as part of the process.

3.1 Hazardous waste generation from pressure vessel section -During cleaning process

Cleaning process involves the preparation of the solvent mixer with water. Mixture of solvent (50% of water and 50% of Methanol) being used in the process. Methanol was being prepared with synthetically. It helps to dissolving the product and water being used to increase the volume for distillation purpose. Some of the product case specific, water was used for dissolving of the product. To optimize the methanol water effluent quantity simulation tool was applied to understand the behavior.

High pressure vessel cleaning was another critical operation due to possible presence of the catalyst. To execute the cleaning operation, inertization was being performed with vacuum nitrogen cycles. Charge Primary Solvent of methanol into High pressure vessel from day tank. Close the High-pressure vessel vent valve. Start the stirrer and raise the temperature up to boiling point. Maintain the High-pressure vessel at same temperature for 2 hours (Note: Vapor pressure inside the High-pressure vessel should not exceed 1.0 Kg/cm^2. Cool the High-pressure vessel temperature to below 35˚C. Unload solvent into spent container and send to spent collection tank. Unload the waste solvent into clean SS container and sample had checked for the specific product content of 10 PPM by using ultraviolet ration method limit of 10 PPM. Equipment was being dried with nitrogen and suitability check for the vessel usage for next product.

Sample was collected after cleaning of the equipment and it was tested with the gas chromatography method. The results were reported and tabulated. Moisture content was varying due to consumption of the water and solvent ratio.

Effluent characteristic- Vessel cleaning			
	Sample-1	Sample-2	Sample-3
Stream-1	Methanol: 50%	Methanol: 49%	Methanol: 53 %
	Water: 50%	Water: 51%	Water: 47%
Stream-2	Methanol: 99%	Methanol: 97%	
	Water: 1%	Water: 3%	

Table 2 Effluent characteristics of vessel cleaning

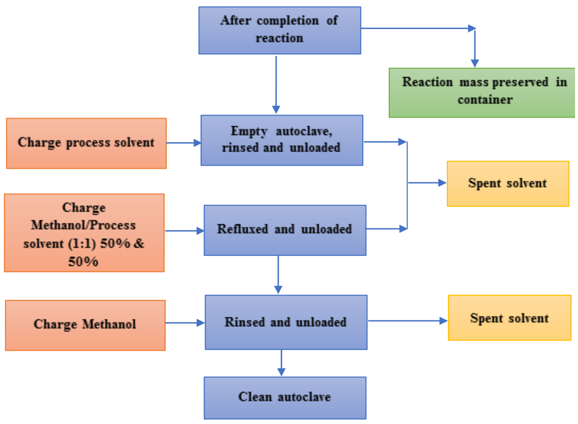


Fig:5 Flow diagram of water consumption and flow pattern

IV. APPLICATION OF DYNOCHEM SIMULATION TOOL TO OPTIMIZE WATER

4.1 Input to the simulation system:

Distillation was one the most commonly used method for liquid waste treatment technologies [5]. For this paper solvent switch for two miscible batch distillation model is used. As part of process and procedure the initial conditions of reaction mass to be defined. The process parameters of water quantity, solvent qty (methanol) and Temperature of the system, Absolute pressure, Non-volatile solutes Quantity, and its molecular weight, density, heat capacity of the solute to be defined. To get defined output from system or end point, the system to be defined as part of procedure. Based on the process requirement distillation end volumes 8lts and distillation time to be obtained. (Attached snap short of dyno chem input model).

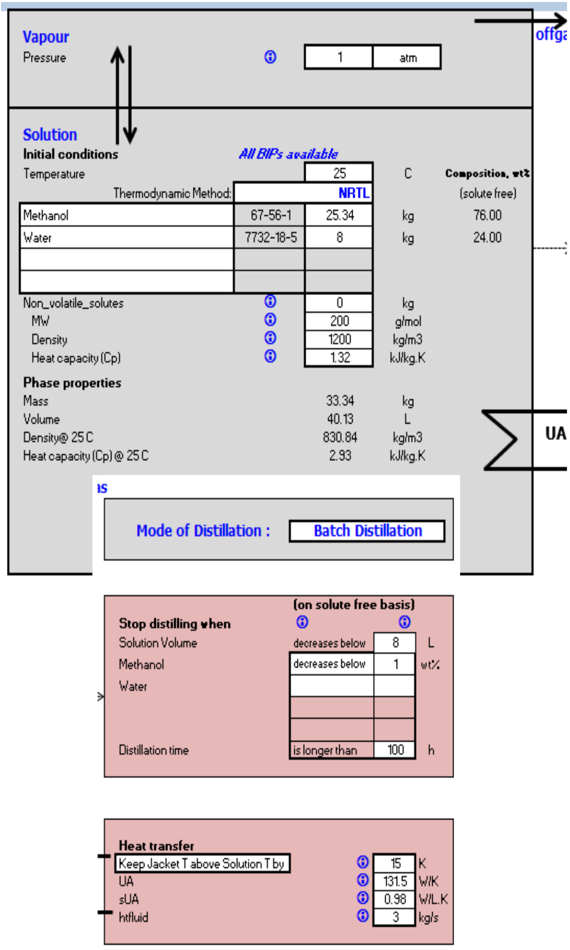


Fig.6 Dynochem input template.

The simulation output was optimized to minimize the energy consumption by distillation as well as water reduction. The test conditions were tested at different Composition of Methanol and water. 40lts of methanol and water mixture is assumed effluent generation from hydrogenation cleaning. And tested at different compositions to minimize the distillation and heating times and water consumption.

Initial simulation was conducted for (methanol/water 20/80 (%v/v)). Variable parameters were predicted as shown in the table 3.

Variable identification by Dyno chem- Simulation tool						
Time	Variables Target Methanol	Variables Current Methanol	Variables Boil up rate	Variables Vmin	Variables Volume at 20C	vapour Pressure
h	wt%	wt%	L/min	L	L	atm
0	1	16.514	6E-16	8	40.044	1
0.051	1	16.514	4.787E-08	8	40.044	1
0.5	1	16.514	1.666E-07	8	40.044	1
1	1	16.514	5.166E-07	8	40.044	1
2	1	11.003	0.0881	8	34.259	1
3.02	1	6.087	0.0777	8	29.003	1
4	1	2.795	0.0699	8	24.633	1
5.061	1	0.9253	0.0648	8	20.432	1

Table. 3 Variable identification by dynochem simulation tool.

Batch distillation time for methanol/water 20/80 (%v/v)) was predicted and inscribed in table. 4.

Batch Distillation (time)- Prediction by Dyno Chem						
time	Solution Water	Solution Methanol	Jacket Temperature	Solution Temperature	Solution Volume	vapour Pressure
h	Kg	kg	C	C	L	atm
0	32	6.33	40	25	40.129	1
0.051	32	6.33	43.116	28.116	40.186	1
0.5	32	6.33	70.517	55.517	40.803	1
1	32	6.33	100.901	85.901	41.483	1
2	29.585	3.658	105.576	90.576	35.534	1
3.02	26.758	1.734	109.159	94.159	30.118	1
4	23.72	0.682	112.086	97.086	25.616	1
5.061	20.149	0.1882	113.983	98.983	21.271	1

Table. 4 Batch distillation predicted by dynochem for (methanol/water 20/80 (%v/v)).

Variable parameters are monitored along with distillation time. It was observed that initial boil up rate is high as compared to end point.

Scenario	Methanol (Vol%)	Water (Vol%)	Distillation time (Hrs)	Heating time (Hrs)
1	20	80	5.06	1.4
2	40	60	5.71	0.83
3	50	50	6.04	1.0
4	80	20	4.57	0.6
5	60	40	5.71	0.83

Table. 5 Testing the simulation output at different methanol/water composition.

Batch distillation time for (Methanol/water 80/20(%v/v)) identified as optimized time for distillation. Water consumption was reduced to 30% v/v for effluent generation.

V. SIMULATION RESULTS.

Model was simulated with varying methanol/water compositions. Final simulation study has been captured and results are displayed in graphical representation. As per the simulation results distillation time for methanol/water (80/20) (%v/v) was minimum and optimized as 4.57hrs, 0.6hrs for distillation time and heating time respectively.

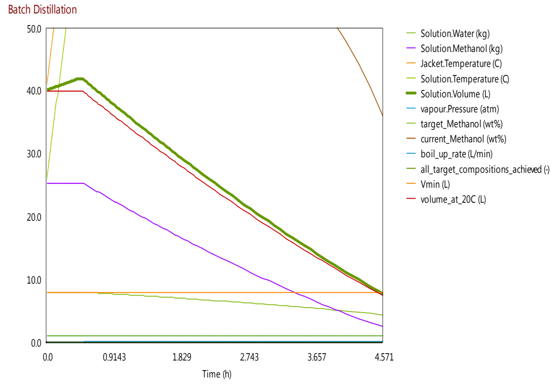


Fig.3 Simulation output

VI. CONCLUSION

In the present study, experimental evidence and results are represented for the wastewater reduction at source point of high-pressure block and recovered water can be recycled for the vessel cleaning. Problem solving approach had designed with the characteristic of the waste and treatment technology had been defined to get recyclable water. It helps to address the effluent generation can be attacked at source and complete treatment cost can be reduced and process become environmentally friendly. The proposed method for the recycle is commercially viable. The concept can be extra plotted to similar kind of water waste and across the pharmaceutical industry. Importunately, mixer of solvent and water had been optimized the ratio by using the dyno chem tool. Various models and logics are simulated and arrived the best possible solution to reduce the waster ration of 20 % of water and 80 % of the solvent. It helps to reduce the water consumption and distillation time also can be reduced based on the simulation toll application. Optimized table had created for the different ratio of the solvent and distillation time. We are calming that based on the simulation tool, distillation time had been reduced which direct benefit of the freshwater consumption in the boiler and energy requirement and wastewater reduction from the steam trap.

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