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Mixing Characteristics in a Conical-based Pharmaceutical Reactor Fitted with a Retreat Curve Impeller

M. HABIB[++], A. R. MEMON*, U. HABIB, M. U. AMIN**, NASEEMULLAH***, A. KHAN, S. NAVEED, M. KHURAM***, S. ALI

Department of Chemical Engineering, University of Engineering and Technology, Peshawar, Pakistan.

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Abstract: Batch stirred tank reactors (STRs) equipped with non-standard impeller designs are commonly used in pharmaceutical industry. The non-standard impeller designs such as retreat curve impellor (RCI) or its modified versions are developed to fit in the irregular shaped STRs like the one with conical base. The non-standard base of STRs is designed to provide ease for final viscous product discharge, cleaning and improving fluid dynamics during the course of mixing and reaction.

In this work, experiments have been conducted in a conical base non-standard STR having a diameter of 0.29 m and equipped with a modified RCI to measure the power number and mixing time by using water and glycerin as working fluids. Visualizations were also performed to gain an insight into the fluid dynamics during the course of the mixing process. Power numbers were measured for different impeller clearance ranges and baffling arrangements. Blending of liquid was observed and measured to occur rather quickly in these nonstandard STRs, which were mainly due to the use of a large RCI impeller.

Keywords: Pharmaceutical stirred tank reactor, power number, blending time, glycerin, water

1. INTRODUCTION

Batch stirred tank reactors (STRs) equipped with integrated heating and/or cooling systems are commonly used in pharmaceutical industry. They offer great versatility for producing small but high value products in batches (Rielly *et al*., 2007). Often they are used to carry a series of different operations such as mixing, heat and mass transfer, chemical reaction and crystallization (Fouad *et al*., 2012). The non-standard STR design development is often based on empirical design equations, scale-up rules and heuristics derived from the experiments conducted in the so-called standard geometry vessels, similar to those which are commonly used in the petrochemical and fine chemicals processing industry (Rielly *et al*., 2007). In standard geometry STR the cleaning and emptying is not a major concern, and so the standard designs are usually based around small diameter impellers *e.g.* Rushton turbine (Han *et al*., 2012), pitched blade turbines and commercial hydrofoils operating in turbulent flow conditions (Yang *et al*., 2013). Often the standard geometry STRs are fitted with four wall baffles, dished bases and fill heights of around one tank diameter. In contrast, many mixing and reaction vessels used in the pharmaceutical sector are glass-lined to provide a physical barrier for corrosion prevention and have partial or no baffling, which are aimed to aid in avoiding the final product contamination. As a result, non-standard impellers such as retreat curve impeller (RCI) may be used, however, their impellor geometries are not covered by the standard correlations in literature which mostly describe the design and assessment of STRs used in chemical or petrochemical industry (Campolo and Soldati, 2002). Furthermore, many such vessels feature conical bases, which are intended for the ease of product discharge that may be operated at relatively low fill levels (Campolo *et al*., 2002). In this regard, RCI designs are often modified to match the conical base such as by angling the blades upwards.

A large proportion of pharmaceutical STRs are used for high viscosity fluid processing operations. For example, blending, reaction and heat transport can bring a gradual change in viscosity of the fluid phase which leads to super-saturation. The subsequent processes of, crystal nucleation and growth, agglomeration and crystal structure breakage are all partly affected by the hydrodynamic environment inside the vessel. Thus this partly determines the overall process yields and final characteristics of the product. The work presented here is intended towards understanding these complex issues, by characterizing the liquid transport, blending times and power requirements evaluated with different viscosity fluids in the conical-based STR vessel.

[++] Corresponding Author: email: enxarm@gmail.com, Phone: 00923333608199
*Department of Chemical Engineering, Mehran University of Engineering and Technology, Jamshoro, Pakistan.
**Khyber Medical University Institute of Medical sciences, Kohat, Pakistan.
***Sarhad University of Science and Technology, Peshawar, Pakistan.

2. MATERIAL AND METHODS

The experimental rig is schematically presented in (**Fig. 1**) and consisted of D = 0.18 m diameter, 3-bladed retreat curve impeller in a see-through conical base STR of T = 0.29 m inside diameter.

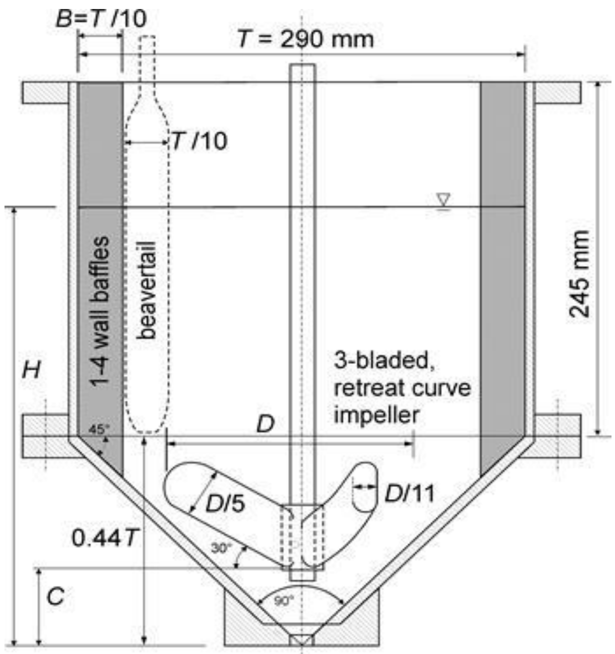

Fig.1: The geometry of the conical based STR, retreat curve impeller, wall baffles and a beavertail baffle.

In this work, liquid filling equivalent to H/T = 1.00 in a maximum STR vessel volume of 20 L was investigated. Effects of various impellor clearances above the base of the cone were also investigated. The conical based STR was surrounded by a transparent rectangular shaped viewing tank filled with water to get an accurate view of the vessel contents. This arrangement ensured clear visual observation of the hydrodynamics inside the STR during its operation. Within the STR, 1 and 4 wall baffles (0.03 m wide and 0.005 m thick) could be installed. The wall baffles were equally spaced in the tangential direction. Alternatively, a single or two 0.03 m wide beavertail baffle with a breadth of 0.01m could be placed in the STR at 0.44 T from the bottom and at 0.1 T from the vessel wall. The STR's top was open to the surroundings. The fluids used in all the experiments reported here were tap water and glycerine. The power requirement of the impellor was premeditated by the spin of the impeller shaft which in-tern was dignified by a Torque Track 9000 digital telemetry system (from Binsfeld Engineering Inc). Strain gauges conveyed the measured signals to an FM transmitter which in-tern were wirelessly received. These were attached on the main impeller shaft and were below the top bearing to eliminate the measurement of frictional effects. First the power number of standard commercially available impellers such as the Rushton turbine (6DT) and pitched blade turbine (PBT) in standard flat-based STR were measured which agreed well with the reported values in the literature (Paul *et al.*, 2004). Mixing or blending time determination is an important variable for any STR design. It is of same significance as the determination of mass transfer or reaction time (Bouaifi and Roustan, 2001). Mixing time indicates about the average velocity, convective transport and bulk motion generated by the liquid pumping of the impellor. The mixing time experiments reported here were done by following the concentration time history of a salt (NaCl) tracer inside the reactor. Mixing time was measured with different geometric arrangements. Initially, a 50 ml salt solution with nearly 1 mass % NaCl was slowly introduced with hand on the top vessel surface. Measurements were then made with the help of a single conductivity probe which had a tip diameter of about 1 mm (Rielly and Britter, 1985). The probe connected to the conductivity meter was housed near the impellor discharge. The conductivity meter sent a voltage signal to the PC data logger at 12 Hz. When the concentration fluctuations measured by the conductivity meter decayed to ±5%, 95% mixing time was recorded. Five repeat experiments for each experimental condition revealed consistent average values of mixing time.

3. RESULTS AND DISCUSSIONS

3.1 Flow Visualizations

The hydrodynamics inside the STR reported in this work were assessed visually. CFD simulations and streak photographs of the exact STR geometry with water as the working fluid is previously reported by Rielly *et al*., (2007). Nevertheless the visualized hydrodynamics inside the STR showed some interesting behaviours as the wall and beavertail baffles did not reach the conical section resulting in the production of a predominant swirling flow due to non-existence of any baffling effect in that region. This resulted in liquid velocity to be predominantly tangential in that region.

Above the conical section, the tangential flow was disrupted even with the use of a single baffle. The baffles converted the tangential flow into the axial and radial components. Due to the chaotic motion of vessel contents with the use of a single baffle, the flow structure was difficult to visualize with the naked eye especially for the low viscosity water; but previous CFD simulations (Rielly *et al.*, 2007; Li *et al.*, 2004; Li *et al.*, 2005; Paul *et al.*, 2004; and Compolo *et al.*, 2002) have reported the existence of a down-flow near the shaft and an up-flow near the vessel boundaries, with weak flow generation near the top fluid surface.

The use of four wall baffles in water showed a slightly disordered flow regime mainly due to the generation of undefined and multiple convection currents in the baffled region with some fluid segregation from the cone below. In almost all cases strong RCI sweep produced tangentially moving liquid currents which moved to the STR walls. Once their contact was developed with the cylindrical wall, the fluid currents changed their path to the horizontal direction depending on the baffling arrangements. Below the impellor no significant vertical loop was observed and the fluid movement was mostly tangential. Any change in the studied C/T values resulted in increasing or decreasing the tangential flow volume in the conical section with little or no impact on the horizontal direction convection currents in the baffled cylindrical section. This is especially in-line with what has been previously reported by Rielly *et al*., (2007).

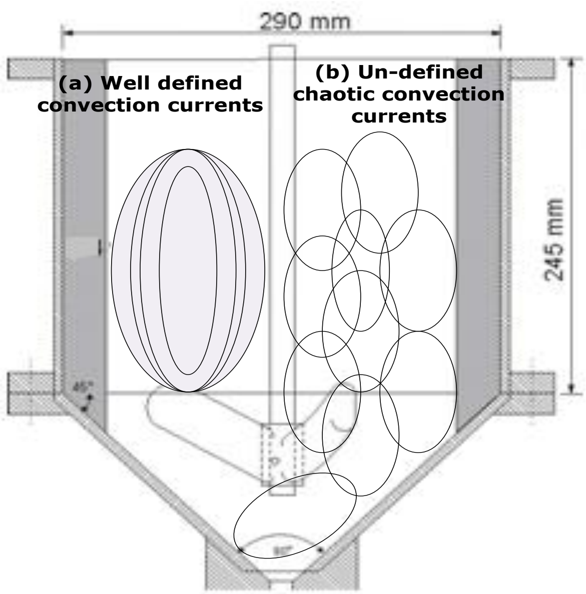

Fig. 2: Well defined and chaotic flow visulised insider the RCI powered STR.

Flow visualizations performed with glycerine showed less chaotic fluid currents mainly due to the introduction of greater viscous forces that played a commanding role to decrease the STR Reynolds numbers. The tangential fluid currents from the RCI sweep were slow to propagate towards the STR walls in comparison to water however, they were observed to show the horizontal convection currents under the influence of wall baffling. The fluid dynamics inside conical base was un-baffled and showed tangentially moving currents. As the glycerine viscosity was reduced to match with that of water, the fluid dynamics inside the reactor became identical to that of pure water. The well-defined and un-defined convection currents reported in the discussion above are mapped in **(Fig. 2)**. It is interesting to note that a change in fluid viscosity such as by using the glycerine as working fluid significantly affected the measured power number and mixing time as will be discussed in the subsequent sections.

3.2 Power Input of the RCI

In this work the power requirements were determined over a range of mixer formations and with Reynolds numbers that ranged from laminar to the turbulent regime ($Re = \rho_L N D^2/\mu_L$, where N is the impeller speed, D is impeller diameter, ρ_L is the density and μ_L is the viscosity of the liquid) with water and glycerin as working fluids. Rielly *et al*., (2007) measured the power number of RCI in a conical based and flat bottom STR with water as working fluid in the turbulent region and reported the power number to remain constant with 4 and 1 wall baffle arrangements. Their investigation showed that for water in turbulent flow regime the conical based STR draw less power in comparison to the flat based STR. In this work an investigation of power number was carried both for laminar and turbulent flow regimes with water and glycerin as working fluids. **(Fig. 3)** shows the relationship of power number with Reynolds number for glycerin and water over a range of fluid viscosities that started with pure glycerin as a working fluid which was gradually diluted to match the viscosity of water at standard conditions of temperature and pressure. It is interesting to note the effect of viscosity on power number; for high viscosity pure glycerin, higher values of power number (2.4 for glycerin) were recorded even at low Reynolds numbers ($<2 \times 10^3$). However, as the glycerin viscosity was decreased to match with that of water the measured power number was observed to fall (0.5 for water). In the water region, a slight decrease in the power number was still observed for Reynolds numbers in the range of 4 to 13 X 10^3; however, it largely remained constant within 5% on either side of the measured mean value. Such behavior for a conical based vessel and RCI is consistent with the standard geometry power number vs Reynolds number curves reported in literature (Paul *et al.*, 2004). For standard geometries it has been reported that power number varies inversely with Reynolds number in the laminar region, then follows a transition, and remains constant in the turbulent region.This is exactly what can be seen in **(Fig. 3).**

In addition to measuring the power number at different viscosities, the conical base effects, fractional baffling effects (1, 2 beavertail baffles and 1, 4 wall baffles) and the impeller clearance effect on power requirements in terms of power number were also investigated. The results of these measurements are shown in (**Fig 4** and **Fig 5)** for water and in (**Fig 6** and **Fig 7)** for glycerin.

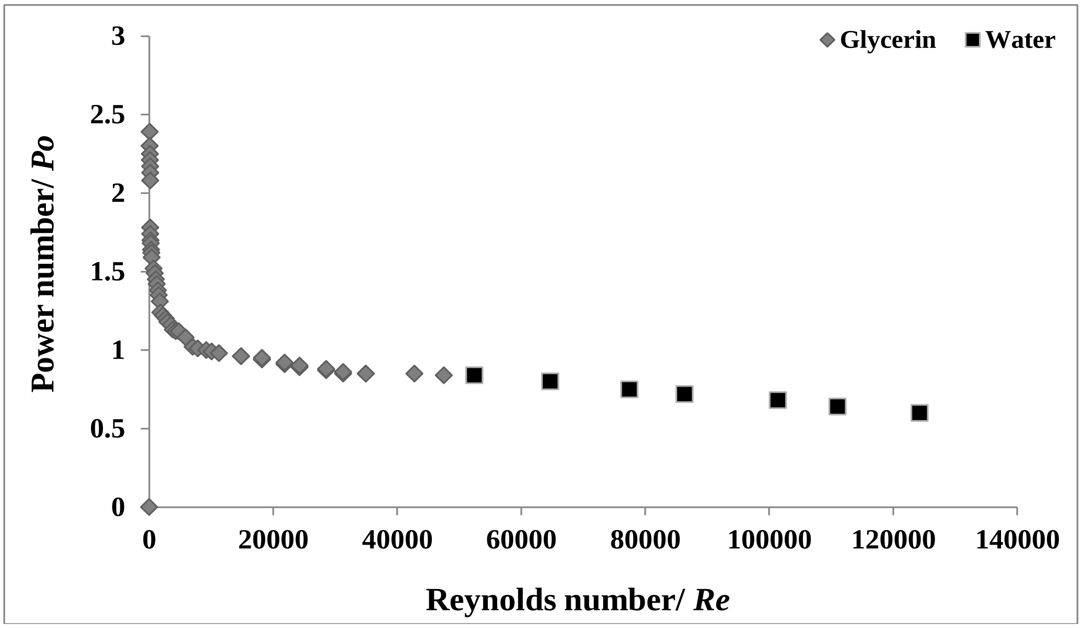

Fig. 3: Power number vs Reynolds number for varying viscosity glycerine and water in the conical based STR with four wall baffles and C/T=0.32.

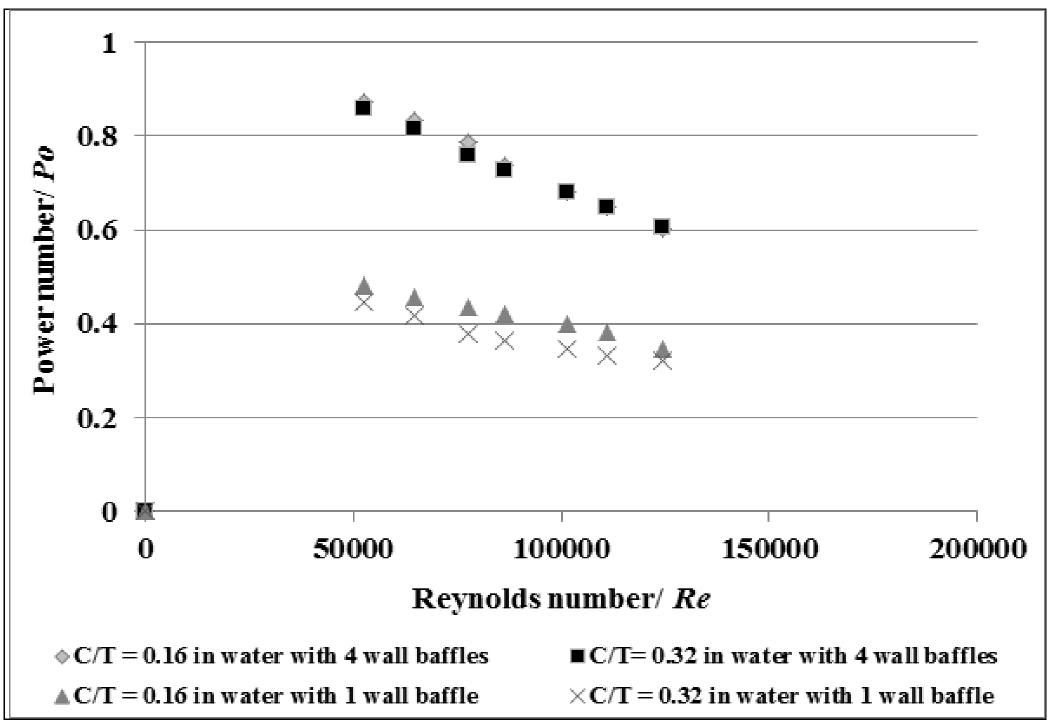

Fig. 4: RCI power numbers with 1 or 4 wall baffles and at two clearance with water.

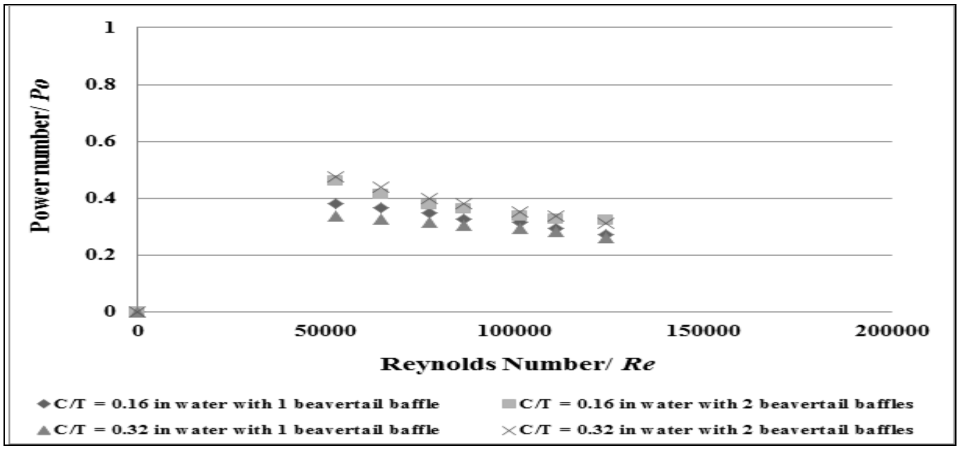

Fig. 5: RCI power numbers with a single and two beavertail baffles at two clearances in water.

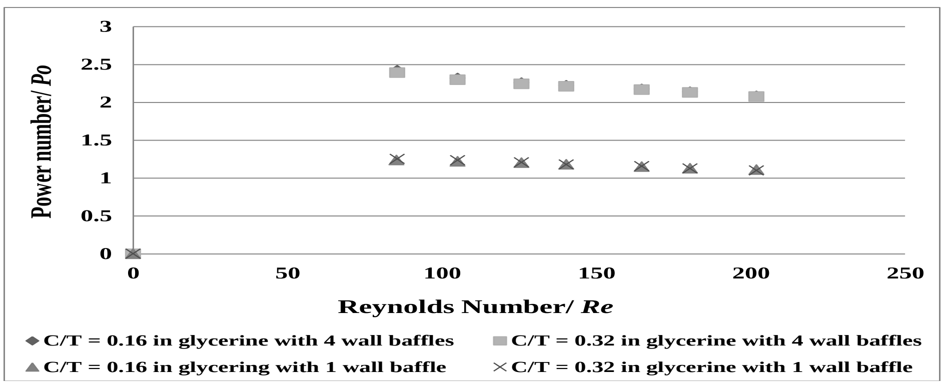

Fig. 6: RCI power numbers with 1 or 4 wall baffles and at two clearances in glycerin.

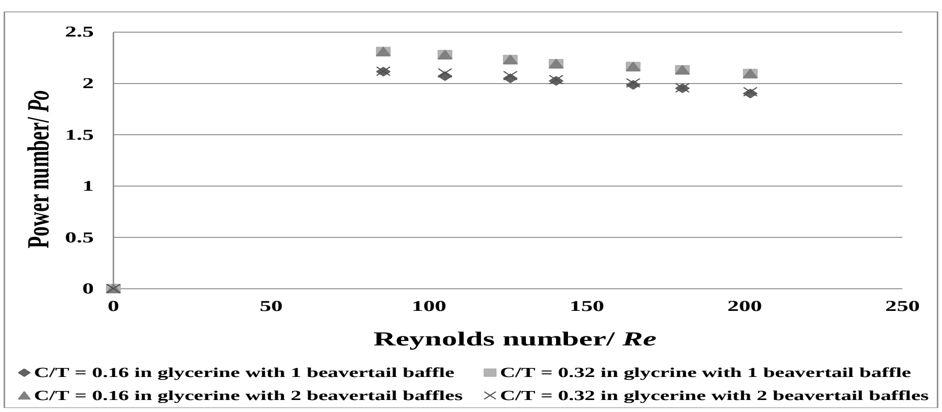

Fig. 7: RCI power numbers with one and two beavertail baffles and at two clearances.

For water in the turbulent region, the measured power number in this work closely matched with that reported by Rielly *et al*., (2007). Campolo (Campolo *et al*., 2002; Campolo and Soldati 2002) has reported the fall of power numbers, *P*0 from 0.79 to 0.70 in the Reynolds's number range of 104 < *Re* < 105 in a laboratory scale STR (with *T* = 0.31 m and *D*/ *T* = 0.58) equipped with three-bladed RCI and two beavertail baffles. This is in contrast to Nagata's (Nagata, 1975) correlation that suggested it to remain constant. In this work the power number ranged from 0.9 to 0.6 for Reynolds number between $5x10^3$ < Re < $2x\ 10^4$ for C/T value of 0.32 and 0.16 with four wall baffles. However with the same operating conditions the power number was observed to drop between 0.5 and 0.3 with the use of a single wall baffle **(Fig. 4)**. The use of beavertail baffles showed the power number to vary in the single wall baffle range **(Fig. 5)**. The use of high viscosity glycerine resulted in an increased power number even at very low Reynolds numbers **(Fig. 6, 7)**. Dickey *et al*.

(2004) have reported a minor decrease in $P0$ with Reynolds number ranges of $104 < Re < 105$ with the use of a $0.1T$ width finger shaped baffle. Studies with Rushton turbine have shown the power number to be independent of impellor to tank diameter ratio. However for a pitched blade turbine power number is shown to depend on impellor to tank diameter ratio (Chapple *et al.*, 2002; Li *et al.*, 2004 and Li *et al.*, 2005). Dickey *et al*., (2004) has reported the measurement of RCI power number by using a single cylindrical baffle. They found the power number to be in-dependent of Reynolds number over the range $Re>10^4$. Hence, looking into the available literature reported above it was expected that the power number would be independent of Reynolds number for an STR containing partial baffling.

In **(Fig, 4, 5, 6 and 7)** a very small effect of impeller clearance is evident however, this is in agreement with Nagata's (Nagata, 1975) power number correlations. Myers *et al*. (2002) reported the reduction of 60% power draw by changing from 4 to 1 wall baffles with a single radial pumping impeller. A similar trend is also evident from **(Table 1)** in case of 1 and 4 wall baffles with water and glycerine as working fluids showing average power numbers at the impellor clearances of $C/T = 0.16$ and 0.32.

Although a reduction in power number for water and glycerine was evident with 4 and 1 wall baffles, the similar effect was nearly non-existent in case of 2 and 1 beavertail baffles with same fluids at the two investigated impellor clearances as shown in **(Table 1)** and in **(Fig. 7)**.

Table 1: Average power numbers over the range $50 < Re < 2\times10^4$ (laminar and turbulent flow) for the retreat curve impeller (RCI) in the conical-based vessel with water and glycerin as working fluids.

Averaged power numbers, P_0				
	Water		**Glycerine**	
Impeller	RCI	RCI	RCI	RCI
Bottom	Conical	conical	Conical	Conical
C/T	0.16	0.32	0.16	0.32
4wall baffles	0.74	0.73	1.95	1.94
1 wall baffle	0.42	0.37	1.03	1.03
1 Beavertail baffle	0.33	0.30	1.76	1.67
2 Beavertail Baffles	0.37	0.39	1.93	1.78

3.3 Mixing or blending time measurements

Before working with RCI, preliminary investigations were carried with a standard geometry PBT down-pumping impeller (Khan *et al.*, 2004) in the flat and conical based vessels to compare the 95% mixing time values with RCI. These trial experiments generated a curve with $N\theta_{95}$ = constant, which is exactly what was suggested by Ruskowski's (1994) generalized correlation shown in eq. (1) below:

$$N\theta_{95} = \frac{5.3}{P_0^{1/3}}\left(\frac{T}{D}\right)^2 \qquad (1)$$

For the pitched blade turbine impeller in a flat-based STR (with $P0 = 1.3$, and $D/T = 1/3$) (Khan *et al.*, 2004), eq. (1) forecasts a $N\theta_{95}$ value of 44, which was in agreement with the initial trail runs made in this work. Measurements made with RCI in the conical-based vessel revealed a 50% drop in dimensionless mixing time values with no dependency on impeller clearances, at the two investigated values, as shown in **(Fig. 8)**. Ruskowski's (1994) correlation can also be written as shown in eq. 2:

$$\theta_{95} = 5.91\left(\frac{\rho V}{P}\right)^{1/3}\left(\frac{T}{D}\right)^{1/3} T^{2/3} \qquad (2)$$

Eq (1) indicates only a small decrease in power input values for PBT by changing from a flat to conical base for a given impeller speed. The volume confined at $H = T$ in the conical-based STR is about 12.8 L (compared with 19.2 L flat-based STR). However eq.(2) indicated that volume differences are in-significant to show a 50% reduction in mixing time. This is in contrast to the observed and recorded values experimentally. The significant reduction in mixing time can be as a result of strong down flows generated by the PBT at low impellor clearances in a conical-based vessel. With RCI, mixing times were measured in the conical-based STR at a number of varying impeller clearances and with different baffling configurations. The results gathered from these measurements are shown in **(Fig. 8 and 9)**.

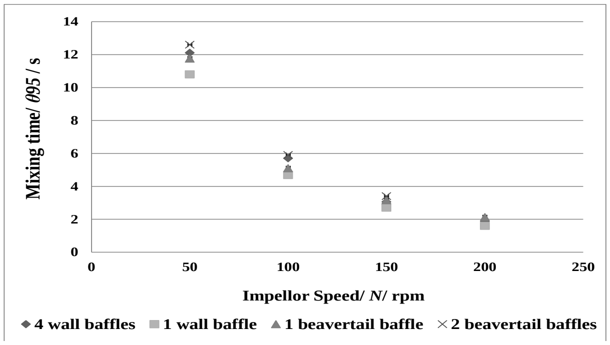

Fig. 8: Effect of baffle arrangements on the 95% mixing time at various speeds for the RCI in a conical-based vessel.

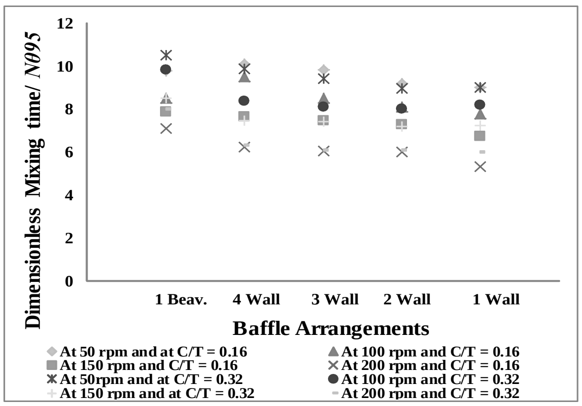

Fig. 9: Dimensionless mixing times for various baffle arrangements at two impeller clearances with water as working fluid.

Dye tracer and flow visualization experiments with different baffling arrangements and impellor clearance values indicated the non-existence of any dead and/or stagnant zones for the Reynolds number ranges investigated in this work. The repeated measurements of mixing time with each geometric configuration revealed the 10% variation of mixing time on either side of the mean value. However the results generally agreed with the Ruskowski's (1994) $N\theta_{95}$ = constant prediction. Almost identical dimensionless mixing time values were recorded for 1, and 4 wall baffle arrangements. In comparison with all other baffling arrangements, four baffles gave the lengthiest mixing times. This is despite the largest power draw by this configuration for any given speed as is evident from **(Fig. 9)**. The use of a single wall baffle gave the shortest dimensionless mixing times, even at high impellor clearance (C/T = 0.32). Approximately the same $N\theta95$ **(see Fig. 9**) value was recorded for all four baffle configurations.

Only small differences in dimensionless mixing times are reported by Myers (Myers *et al.*, 2002) for radial, and mixed axial discharge impellers with 1 to 4 wall baffles. The weak minimum was reported for 2 baffles. Others (Kumaresan *et al.*, 2005) have recorded minor decreases in dimensionless mixing time values when the number of wall baffles was increased from 2 to 6. **(Fig 9)** shows the elongated mixing time values for a single beavertail baffle, which might be due to the generation of strong radial and axial flow components in the baffled region, but had little effect on the swirling flow in the conical section. This suggests the inefficiency of single beavertail baffle for liquid mixing based on this investigation in a conical based STR. In short, the conical-based STR arrangements explored in this investigation have revealed very short mixing times. Based on the measurements it can be safely concluded that at high Reynolds number flow ranges the partial baffling in the conical-based STRs will not lead to any severe mixing problems.

Equation (1) shows that an increase in D/T ratio will result in significantly decreasing the dimensionless blending time. This can be one of the main reasons for RCI to remain effective for liquid mixing, despite the use of less number of baffles. The experimental data gathered from this work concludes that a simple constant correlation for all impellor types cannot be used to predict the dimensionless mixing time of an RCI by changing from a flat to conical based STR.

4. CONCLUSION

In this work a conical based STR equipped with an RCI was used to measure the power number and dimensionless blending times with water and glycerin as working fluids. As is the case with the most standard geometry STRs, the measured power number of RCI was not much affected by the impeller clearances even with the use of different viscosity fluids. In this work, significant dependency of power draw was observed on the number wall baffling however the effect tend to reduce with the use of a single and/or two beavertail baffles even in the same vessel geometry. Blending times predicted by Ruszkowski's correlation gave relatively unadventurous approximations for the RCI in the conical based STR. Generally, a single wall baffle gave comparatively small mixing times. The longest $N\theta95$ values were recorded for a single beavertail baffle. In the turbulent regime for almost all cases, the experimentally measured dimensionless blending times were comparatively short indicating that the mixing at macro-scale will least effect the operation of a conical based STR.

REFERENCES:

Bouaifi, M. and M. Roustan (2001) "Power consumption, mixing time and homogenisation energy in dual-impellor agitated gas-liquid reactor", Chemical Engineering and Processing, **(40):** 87-92.

Campolo, M., A. Paglianti and A. Soldati (2002) "Fluid dynamic efficiency and scale-up of a Retreated blade impeller CSTRs", Eng. Chem. Res., **(41):** 164Pp.

Campolo M. and A. Soldati (2002) “Appraisal and fluid dynamic efficiency of Retreated-blade and Turbofoil impellers in industrial-size CSTRs”, Ind Ind. Eng. Chem. Res., **(41):** 1370Pp.

Chapple, D., S. M. Kresta, A. Wal, and A. Afacan (2002), “The effect of impeller and tank geometry on power number for a pitched bladed turbine”, Trans IChemE, Institution of Chemical Engineers, (80), Part A, 365Pp.

Fouad, Y.O., G.F. Malash, A.A. Zatout, and G. H. Sedahmed (2013), “Mass and heat transfer at an array of vertical tubes in a stirred tank reactor”, Chemical Engineering Research and Design **(91):** 234-243.

Han, Y., J. J. Wang, X.P. Gu, and L. F. Feng (2012), Effect of agitation on the fluidisation behaviour of a gas-solid fluidised bed with a frame impeller”, Chemical Engineering Science **(74):** 9-17.

Khan F. R., C. D. Rielly, and G. K. Hargrave (2004) "A Multi-block approach to obtain angle-resolved PIV measurements of the mean flow and turbulence fields in a stirred vessel", Chem. Eng. Technol. **(27):** 264Pp.

Kumaresan, T., N. K. Nere, and J. B. Joshi (2005) "Effect of internals on the flow pattern and mixing in stirred tanks", Ind. Eng. Chem. Res. **(44):** .9951Pp.

Li, M., G. White, D. Wilkinson, and K. J. Roberts (2005), “Scale up study of retreat curve impeller stirred tank using LDA and CFD”, Chem. Engg. Journal, (108) Issues 1-2, 81Pp.

Li, M., White, G. and D. Wilkinson (2004), “LDA measurements and CFD modelling of a stirred vessel with a retreat curve impeller”, Ind. Eng. Chem. Res., **(43):** 6534Pp.

Dickey D. S., K. J. Bittorf, C. J. Ramsey, and K. E. Johnson (2004), “Understand flow patterns in glass-lined reactors”, Chem. Eng. Progress Magazine, 21Pp.

Myers K. J., M. F. Reeder and J. B. Fasano (2002) “Optimize mixing by using the proper baffles”, Chem. Eng. Progress Magazine, 42Pp.

Nagata, S. (1975) “Optimize Mixing by Using the Proper Baffles”, Mixing: Principles and Applications, Halstead Press, Tokyo. Japan.

Paul, E. L., V. A. Atiemo-Obeng, and S. M. Kresta (2004), “Handbook of industrial mixing”, Wiley Interscience, John Wiley and Son, Inc., Hoboken, New Jersey, USA.

Rielly, C.D., M. Habib, and J. P. Sherlock (2007), “Flow and mixing characteristics of a retreat curve impeller in a conical-based vessel”, Chemical Engineering Research and Design, (85): A7, 953-962.

Rielly, C. D. and R. E. Britter (1985), “Mixing of passive tracers in stirred tanks”, 5th Euro. Conf. on Mixing, Wurzburg, FRG, BHRA Fluid Eng. 365Pp.

Ruszkowski, S. (1994) "A rational method for measuring blending performance and comparison of different impeller types", 8th Euro. Conf. on Mixing, Inst. Chem. Engrs. Rugby, U.K., 283Pp.

Yang, L., J. Cheng, P. Fan, C. Yang, and Z. Mao (2013), “Micromixing of solid-liquid systems in a stirred tank with double impellers”, Chemical Engineering and Technology, Accepted Manuscript, Article in Press, DOI: 10.1002/ceat.201200406.