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Static Mixture-Right Candidate Tool for Enhancing the Flow Chemistry- A Review

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ABSTRACT: A static mixer is precision engineered proven process intensification equipment, for homogenizing the process fluids and for intensifying the reaction kinetics. This review paper will aid researchers to gain insight about various parameters affecting the intensification rate of flow chemistry. Effect of the order of the reaction on positioning the static mixer relative to continuous stirred tank reactors were discussed elsewhere in this paper. Finally, couple of Active pharmaceutical ingredients (API) synthesis in flow mixer waswell discussed in brief. Recent advances in the design aspects were summarized in details. Eventually, this article can be used as quick reference guide for practicing chemist and chemical engineers.

KEYWORDS: Static mixer, Plug-flow reactor, Reaction rates, Process intensification, Pressure drop, Reynolds number.

I. INTRODUCTION

In general, static mixture is made of cylindrical tube housing rectangular plates twisted around 180° as they make double helix structure, as shown in the figure 1. Static mixer (motionless mechanical mixer) traces back history in 1965), by Arthur D little company. Recently, use of static mixers has relatively increased in pharmaceutical industries. However, advantages of this relatively inexpensive technology are not significantly exploited yet by industries. Desired reaction rates are obtained at least possible pressure drops when compared to conventional mixers. They cater wide range of applications mixing, blending, gas-liquid contacting, viscous reaction, heat and mass transfer augmentation, dispersion, emulsification and extraction.

Plug flow reactors renders a confined pathway for the process fluid, where some critical reactions, involving high pressure, potentially toxic or explosive intermediates shall be performed, safely, compared to conventional batch and semi-batch reactors [1]. Flow chemistry refers to plug flows, where the reactive components are pumped through or re-circulated continuously. Eventually, it will be right to term the static mixers as modified plug flow reactor. Continuous flow chemistry shows significant increase in process intensification rate compared to traditional one-pot solution processing condition [2]. Citing the article in Wikipedia, eventually, in laminar flow (<2300), a processed material divides at the leading edge of each element of the mixer and follows the channels created by the element shape, as displayed in Figure 1(a). At each succeeding element, the two channels are further divided, resulting in an exponential increase in stratification. The number of striations produced is 2^n where 'n' is the number of elements in the mixer. Given the case 20 elements, over 1 million layers are created. For flow greater than > 4000 , main mixing is combination of flow conversion and inversion, as displayed in Figure 1(b)

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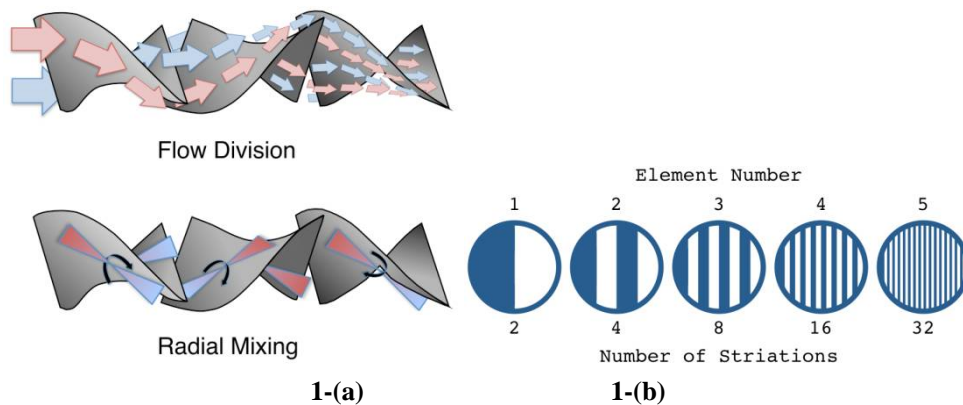


Figure 1(a): Depiction of how flow division and radial mixing can occur in a static mixer.

Figure 1(b): Flow division in a static mixer that uses baffles is a function of number of elements in the mixer as cited in Wikipedia.

Basic equation relating the pressure drop and friction factor, are given below

$$f = \frac{\Delta P D}{\frac{1}{2} \rho L v^2} \text{-----(1)}$$

$$f = \frac{64}{Re} \text{-----(2)}$$

$$V = \frac{4Q}{\pi D^2} \text{-----(3)}$$

Equation 1 concerns with laminar Darcy friction factor and equation 2, over range of Reynolds number. Where ΔP refers to pressure drops across the length of the static mixer tube. V- Mean velocity and Q volumetric flow rate are related in equation 3. Helical shaped mixing element has several advantages over other mixing elements, such as lowest pressure drop per mixing element, suitable for low and high viscous materials, can handle big solid particle/diameter, clean-in-place and sterile –in-place applications.

II. PARAMETERS AFFECTING THE EFFICACY OF STATIC MIXING

The parameters affecting the efficacy of static mixers are flow rate, nominal diameter, shape and number of mixing element, material of construction, nature of precursors, pressure drop, length of static mixer, viscosity and density. Mushtak et al, [4] conducted flow visualization studies to observe the effectiveness of mixing in static mixer. Friction factor variation with Reynolds number is displayed in figure 2. They observed that given the case of four mixing elements, the dye was found to be well mixed as it traverses the path shown in the figure 3. It is well evident that as the Reynolds number increases from 160 to 830 the mixing quality is observed to be significantly enhanced. With reference to figure 3 as number of mixing element increases, the visual homogeneity is reached even at low Reynolds number which is around 400 for 8 mixing element and 60 for 12 mixing element.

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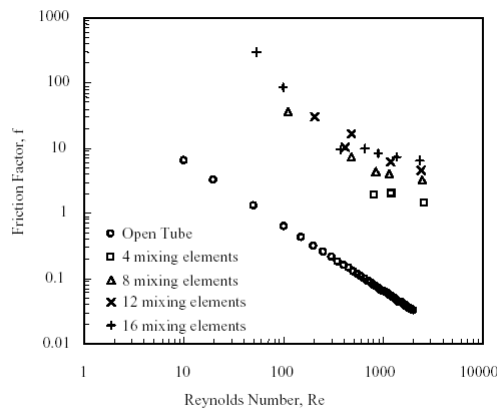


Figure2 : Friction factor variation with Reynolds Number[5]



Figure 3: Flow visualization Results, (a,b,c,d), 8 Mixers (e&f) 12mixers (g) flow right to left.

III. RIGHT POSITIONING OF STATIC MIXER FLOW REACTOR (PLUG FLOW REACTOR)

Author wish to cite the Octave Levenspiel's[5] recommendation for best arrangement of set of ideal reactors, for reactions whose rate-concentration curve rises monotonically (any n -th order, $n > 0$) the reactors should be connected in series. For the order ($n > 1$), the placement should be plug-flow, small mixed tank reactor, and large mixed tank reactor. For order $n < 1$, placement protocol should be reversed. For ideal position of static mixer, author suggests for order ($n > 1$), static mixer, shall be Placed first, followed by small mixed tank, and large mixed tank later, as displayed in figure 4. For order ($n < 1$), above mentioned protocol shall be reversed.

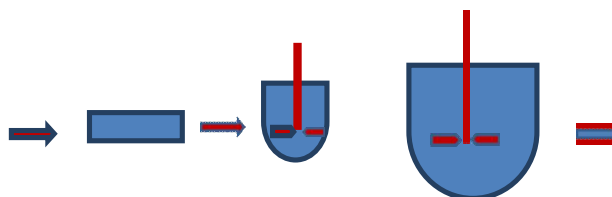


Figure 4: Order ($n > 1$), Left to right, Static mixer, small mix tank, and large mix tank.

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IV. ACTIVE PHARMACEUTICAL INGREDIENT (API) SYNTHESIS IN FLOW MIXERS

Recently, Jamison's lab[3] reported improved flow synthesis of Ibuprofen sodium salt as displayed in figure 5, that delivers target compound within three minutes of residence time, with an improved productivity of 135 mg/min. Here again, the key steps are as in Friedal craft acylation, 1,2 aryl migration and saponification). Their research focuses on improved output by intensifying over all reaction.

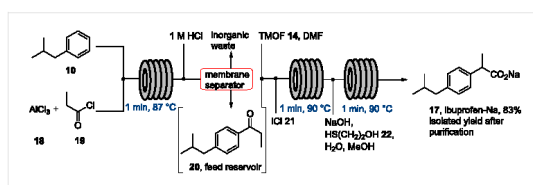


Figure 5: Jamison's flow synthesis of sodium salt [4].

The re-development and commercialization of laboratory based tube-in-tube reactor by the lay group in 2009 [3], observed to be significant advancement in flow chemistry as displayed in figure 6. Eventually, this enabled wider use of gases and volatile compound, depending on intended application. The gaseous fluid can be fed either into the inner or the outer tube, and upon pressurization penetrates into the reagent stream, where the desired reaction occurs. They got to observe, applied vacuum enabled the extraction of gaseous substance from flow stream. Flow synthesis of the anti-inflammatory agents fentanyl, as displayed in figure 7, in which ammonia gas was fed into inner tube, whilst outer tube contains a solution of Phenethylisothiocyanate and dimethoxy ethane.

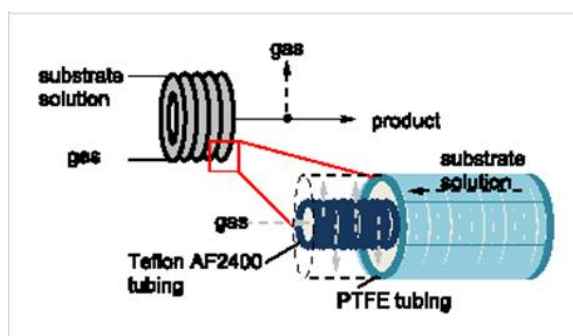


Figure 6: Schematics of Tube-in-Tube reactor [4]

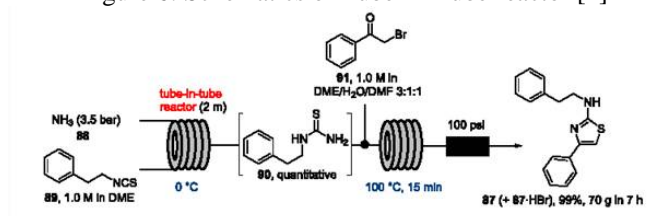


Figure 7: Flow synthesis of fentanyl via tube-in-tube reactor system [4].

V. RECENT ADVANCES IN STATIC MIXTURE

Recently in 2017, [6] group of researchers have developed catalyst coated 3-D printed static mixer, which are used as insert in the plug flow reactors, as displayed in figure 8. They did prepared the base material in Ti alloy, COCl Alloy,

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Al-alloy, SS 316 alloy using 3-D metal printer. The catalysts were then applied using either electro-deposition or metal cold-spray techniques, and evaluated in continuous flow hydrogenations.

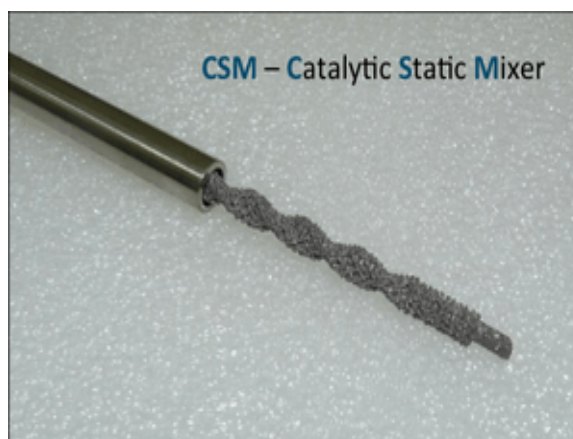


Figure 8. Catalytic Static Mixer insert

These Researchers coated Ni, Pt, Pd, Cu, and Au onto the bare base substrate, successfully. It has been reported elsewhere, [7-10], the kinetics of polymerization reaction shall be intensified using 3-D printed static mixture. Theo. K. Schulpen[7], did experimentally study, performance of two types of static mixers of 6 mm diameter, manufactured by 3D metal printing method. Efficacies of CSM vs. various parameters like pressure drop, mixing, heat transfer, and residence time were experimented by him. He observed that Pressure drop is in line with bigger diameter static mixers. Mixing performance did depend on flow rate and density difference of mixing fluid in addition to viscosity ratio parameter. Rate of heat transfer was observed to be significantly higher compared to conventionally design static mixer. The residence time distribution is characterized by a constant value of the dimensionless radial dispersion coefficient (Fourier number).

VI. CONCLUSION

Efficacy of the static mixer over conventional mixers was well presented in detail. The effect of number of mixing elements vs rate of homogenization was discussed in brief. Readers of this article will eventually get an idea of alignment of static mixture in right protocol, based on the order of the reaction. The importance of flow chemistry in API formulation was discussed citing recent literature references as well. Recent advances like catalytic static mixer were discussed briefly. In general, this review paper will give basic insight about static mixer for practicing engineers and chemist.

NOMENCLATURE

API-Active Pharmaceutical Ingredients
PTFE-poly tetra fluoro ethylene
HBR HydrogenBromide
NH₃. ammonia
DME-Dimethoxy ethane
DMF-Dimethyl formamide
NCS-N-chlorosuccinimide
NaOH-sodium hydroxide
AlCl₃. aluminum chloride
TMOF-Trimethylorthoformate
HS(CH₂)₂OH- 2 Merkaptoetanolis

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HCL-hydrochloric acid
PSI-pressure per square inch
Re-Reynolds number
f- friction factor
 ΔP -Pressure drop
 ρ -Density (g/cc)
Q-Volumetric flow rate
V-mean velocity (m/sec)
L- length(m)
D-nominal diameter (m)
n-order of the reaction.
vs.- verses
SS-stainless steel
COCl-cobalt chloride
Al –Aluminum
n-order of reaction
3-D three dimensional
Ni-Nickel
pt-platinum
pd-palladium
Cu- copper
Au-Gold
CSM-catalytic static mixer

REFERENCES

- [1] Riccardo Porta, mauizioBenaglia, Alessandra Puglisi, "Flow chemistry: Recent Development in the synthesis of pharmaceutical Products, Organic Process research and development", Vol.20,pp. 2-25, 2016.
- [2]Junyong Zhang, Chnhua Gong, XianghuaZeng, JingliXie, "Continuous Flow chemistry: New Strategies for Preparative inorganic chemistry, Coordination Chemistry Review",Vol 324, pp. 39-53, 2016.
- [3] Marcus Baumann and Ian R. Baxendale, "The synthesis of active pharmaceutical ingredient (API) using continuous flow chemistry",Beildstein J. Organic Chem,Vol 11 ,pp. 1194-1219, 2015.
- [4]MushtakAl-Atabi, Yosuf AAbakar, "Laminar Mixing in SMX static mixer",Journal of Engineering science&Technology", Vol 2.No1,pp. 95-101, 2007.
- [5] Octave levenspiel, "Chemical Reaction engineering", Third Edition, ISBN 9971-512-41-6, p .135, 2001.
- [6] Avril,A., Hornung,C.,Urban.A.J., Fraser.D.,Horne.M.m., Veder.J.P, Tsanaktisidis.J., Rodopoulos.T., Henry.C., and Gunasegaram.D., "Continuous flow hydrogenations using novel catalytic static mixers inside a tubular reactor", React. Chem. Eng., 2016.
- [7] Theo.K. Schulpen, "Performance of 3-D Printed Static Micro-Mixers for Polymerisation Reactions",Aiche Annual Meeting, Nov 8-13, , www.aiche.org/annual, 2015.
- [8] Ghanem, A., Lemenand, T., Della Valle, D., Perhossaini, H., "Static Mixers: Mechanisms-Applications, and Characterization Methods - A Review".Chemical Engineering Research and Design.Vol. 92, ,pp. 205 - 228 , 2014.
- [9]Tien, N.K., Flaschel, E., Renken, A., "Bulk Polymerisation of Styrene in a Static Mixer", Chemical Engineering Communications, Vol. 36, 1985.[10]Naumann, E. Bruce, "Chemical reactor design, optimization, and scale-up",MGH, Chapter 8, 2002.

BIOGRAPHY

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