CHEMICAL ENGINEERING RESEARCH AND DESIGN 90 (2012) 750–756

Contents lists available at SciVerse ScienceDirect

Chemical Engineering Research and Design

journal homepage: www.elsevier.com/locate/cherd

Observations of solid–liquid systems in anchor agitated vessels

M.S. Abhishek[a,b], *Suvarna Choudhari*[b,*], *Frans Muller*[c]

[a] *Department of Chemical Engineering, Siddaganga Institute of Technology, Tumkur, Karnataka, India*
[b] *AstraZeneca India Pvt. Ltd., Pharmaceutical Development, Bellary Road, Bangalore 560024, Karnataka, India*
[c] *University of Leeds, School of Process, Environmental & Materials Engineering, University of Leeds, Leeds LS2 9JT, UK*

ABSTRACT

Although process development is often done in well agitated vessels (e.g. with a retreat curve, pitched blade turbine etc.), there are a sizeable number of contract manufacturers' still deploying a significant number of anchor agitated process units. For the purpose of observing the Zwietering constant value 'S' and few industrially important solid–liquid systems, we conducted extensive suspension experiments with anchor agitated vessels for varying *D*/*T* ratios (0.74 and 0.73). In this study, Zwietering's N_{js} (just suspension speed) and the corresponding 'S' factor were obtained for each system over a range of solid loadings. We found that the Zwietering constant was strongly dependent on the nature of the solid–liquid system; i.e. different systems had different 'S' values for the same geometrical configuration.

Keywords: Zwietering constant (S); Just suspension speed (N_{js}); Anchor agitator; Solid–liquid mixing

1. Introduction

Solid–liquid mixing is important in agitated vessels during process development and further during scale-up. A lack of understanding of mixing can lead to serious process failures when accommodating and/or scaling up a process in alternative equipment. For instance, during bond formation for many organic compounds nucleophiles are generated in the presence of a strong base like cesium carbonate to react with electrophiles. Cesium carbonate suspended in an organic solvent is thus frequently used in pharmaceutical transformation reactions like C, N, S, O alkylation, condensation and metal catalyzed coupling reactions (Flessner and Doye, 1999). As cesium carbonate is very dense (4072 kg/m^3), it settles relatively quickly and the reaction rate for impeller speeds below just suspension speed (N_{js}) is often significantly slower than for reactions wherein impeller speeds are above N_{js}. Thus, achieving the right solid–liquid suspension in an agitated vessel is very critical to scale-up of these reaction systems. Inadequate S–L mixing can result in lower quality and yields. The impact of this may be very expensive, especially if shortage of material leads to a delay in the clinical program.

In AstraZeneca, process development is typically done in 100 ml–5 l jacketed glass reactors using a range of agitators; usually glass pitched blade or retreat curve impellers. These reactor systems are a "scale down" of the larger plant vessels in our multipurpose drug substance manufacturing facilities. At the large scale, agitation is provided by glass lined impellers to ensure chemical resistance and ease of cleaning, typically these have retreat curve impellers but over the last decennia's a wider range of glass lined impellers has become available. Anchor agitation systems are not commonly used in AstraZeneca, but frequently used, for instance, by our Asian contract manufacturing partners. Based on internal survey results, approximately 60% of the multipurpose batch reactors in Indian pharmaceutical industries have anchor and paddle agitators. This is exemplified in Fig. 1 which shows agitator's systems from two of our larger Asian outsourcing partners.

As a result of the different prevalent type of agitator, processes developed in AstraZeneca will thus be scaled up to vessels with anchor agitators, even though these might not be the systems of choice for our processes, especially those in which solid–liquid mixing is important as in the aforesaid cited examples.

* *Corresponding author*. Tel.: +91 80 23621212/15; fax: +91 80 23622011; mobile: +91 9902018465.
E-mail address: Suvarna.choudhari@astrazeneca.com (S. Choudhari).

Received 22 June 2011; Received in revised form 28 September 2011; Accepted 29 September 2011
0263-8762/$ – see front matter © 2011 The Institution of Chemical Engineers. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.cherd.2011.09.018