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Comparison of torque method and temperature method for determination of power consumption in disposable shaken bioreactors

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Abstract

Disposable bioreactors are increasingly used in bioprocess development of animal cell cultures. However, the engineering parameters of the present disposable bioreactors are very difficult to characterise. Characterisation of any bioreactor is important to evaluate the suitability of operating conditions and absolutely necessary for successful scale-up. In this research work, an attempt is made to validate a characterisation method which is simple and can be used for any given volume of disposable bioreactors larger than 2 L. Two evaluation methods, namely the temperature method and the well established torque method were used for determination of power consumption in 2 L and 20 L disposable shaken bioreactors. The trend of the values of power consumption was shown with respect to shaking frequency and filling volume. Results indicate that quite reasonable values of power consumption can be obtained by the temperature method and the torque method, which are in good agreement with each other (error <30%).

Keywords: Bioprocess development; Disposable; Shaken bioreactor; Characterisation; Power consumption; Torque; Temperature; Validation

1. Introduction

The very first use of disposable shaking bioreactors was shown by Falch and Heden [1] who cultivated microbial cells in 300 mL tetrahedron bags. In recent years, plastic made disposable bioreactors have been successfully used for cultivation of cell cultures for protein production from developmental stage to production stage [2–4]. The disposable-based concept has a big advantage of time and capital cost saving because no cleaning and validation is required. It was proven that initial capital investment could be reduced by 60% of that for standard stainless steel fermenters [5]. Moreover, cleaning and SIP validation reduced to almost 66% [6,7]. However, there is still a shortage of fully characterised disposable-based cGMP-compliant manufacturing unit.

Shake mixing has been widely used at small scale level in biotechnology laboratories and industries [2,8,9]. Their simple operation, easy handling and low cost are some of the major advantages. Buechs et al. have extensively characterised conical shaken vessels (Erlenmeyer flasks) up to the size of 5 L [10–13]. They have shown that local energy input or power consumption is more evenly distributed in shake mixing than in standard stirred mixing [11]. Thus, hydromechanical stresses are lower in shake mixing than in stirred mixing. Therefore, shaken bioreactors are generally very suitable for the cultivation of cells sensitive to hydromechanical stress, like animal or plant cells. This was proven by Liu et al., who cultivated many kinds of animal and insect cell cultures in cylindrical shaking bioreactors at pilot scale [2]. In spite of successful cultivation of animal cells in 20 L and 60 L shaking bioreactors, Liu et al. emphasised on detailed characterisation of these bioreactors. Characterisation of any kind of bioreactor gives more defined operating conditions, which is also a very important criterion for successful scale-up.

Power consumption is one of the most important criteria of successful scale up. It has direct influence on mass transfer as well as hydromechanical characteristics. Power consumption and its distribution in the culture liquid is already known for conical shake flasks up to the size of 5 L [13]. The authors used two different torque methods which provided accurate and reliable results. However, because of quite different geometry the results cannot be extrapolated to cylindrical vessels. Moreover

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Nomenclature

A	heat transfer area (m^2)
C_p	specific heat (J/kg K)
m	mass of a liquid (kg)
M	torque (Nm)
n	shaking frequency (rps)
P	power consumption (W)
t	time (s)
T_f	liquid temperature (K)
T_o	room temperature
UA	overall heat transfer coefficient (W/K)
V_L	filling volume (m^3)
z_k	number of flasks

a maximum of 20% of the total flask volume was used as filling volume in their work. Kato et al. have characterised cylindrical vessels over a narrow range of operating conditions up to 20 L [14]. They used an electrical method for determination of power consumption. This method has a lower accuracy and may not be reliable due to unknown losses of energy in the electric drive. In a different work Kato et al. also measured power consumption by the temperature method in 20 L cylindrical shaken bioreactors [15]. Results obtained with the electrical method were extrapolated and compared but they gave far higher values than the actual values of power consumption [15]. Sumino et al. measured the value of power consumption in small baffled and non-baffled shake flasks by the temperature method [16].

Till date it was assumed that the temperature method can be used but the accuracy of this method was unknown in comparison to other validated methods like the torque method. In the present work both torque and temperature method are used for the determination of power consumption in 2 L and 20 L disposable shaking bioreactors. Thus, an attempt is made to prove the validity of the temperature method.

2. Materials and methods

For all the experiments 2 L polycarbonate (PC) bottles and 20 L polypropylene (PP) bottles (Nalgene, USA) were used. A table-top shaker (LS-W, Kuehner AG, Switzerland) was used to impart shake mixing. For the determination of the power consumption using the temperature method in 20 L vessel, a commercially available shaker RC-6 (Kuehner AG, Switzerland) was used. All the experiments were performed at 50 mm shaking diameter and water was used as a fluid.

2.1. Torque method

Power consumption in 2 L and 20 L disposable reactors mounted on a shaker table was measured by the method developed by Buechs et al. [13]. The method is based on the measurement of the torque developed by the liquid which rotates around the axis of the vessel. The torque is generated on the axis

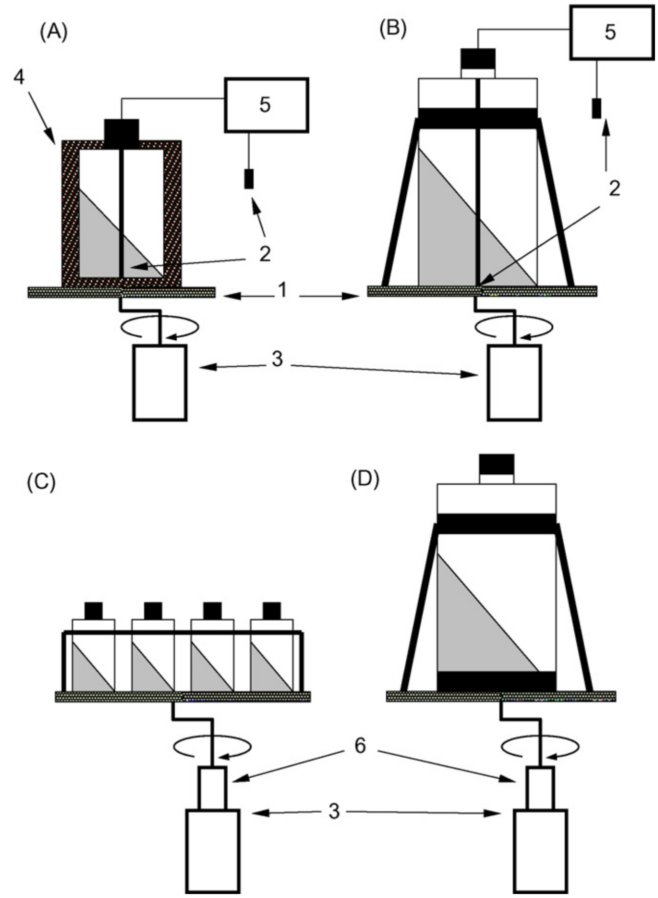

Fig. 1. Measurement of power consumption using the temperature method in (A) insulated 2 L cylindrical shaking vessel, (B) non-insulated 20 L cylindrical shaking vessel. Measurement of power consumption using the torque method in (C) 2 L cylindrical shaking vessel and (D) 20 L cylindrical shaking vessel. (1) Shaking table, (2) temperature sensors, (3) motor, (4) heat insulation, (5) digital multimeter, and (6) torque sensor mounted on motor.

of the motor. Mechanical friction losses and wind resistance of the vessel are compensated by measuring the torque generated by a dead weight which should be the same as that of the rotating liquid and the vessel. The power consumption can then be measured by following equation:

$$\frac{P}{V_L} = \frac{(M_1 - M_2)2\pi n}{z_k V_L} \qquad (1)$$

where M_1 is the torque developed by rotating liquid and M_2 is the torque developed by the dead weight. Fig. 1C and D shows the arrangements used for torque measurement for 2 L and 20 L vessels, respectively. As shown in Fig. 1C, four 2 L PC bottles instead of one were mounted on the shaker table to maximise the accuracy in the torque measurements. The shaker was rotated by the external motor which had an integrated torque sensor (ViskoPakt, HiTech-Zang, Germany). The control of this motor was automated by a LabView software (National Instruments, Germany) which also recorded the data from the torque sensor. Fig. 1D shows the same arrangement for a 20 L PP vessel. To keep the torque produced within the limits of the torque sensor (0–1 Nm) only one 20 L vessel was used. Measurements were