SPORE POLYMER CHALLENGE OF THE ALP MODEL 624 BFS MACHINE

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Introduction

Extrusion of polymer to form the primary container is a critical element of the BFS process given that the interior of the extruded container is in direct contact with filter sterilized or bulk sterilized product. An earlier exploratory study[1], utilizing spore contaminated polymer, provided evidence of heat lethality associated with the extruder process. Polymer homogenization (i.e. distribution within the extruded polymer mass) combined with heat lethality are thought to contribute to the ability of the BFS process to provide a final product free of viable microorganisms (i.e. sterile). A collaborative study involving Automatic Liquid Packaging, Inc. and Air Dispersions Ltd. has been carried out to further the understanding of the single screw extrusion process and its impact upon microbiological quality of BFS product.

Description of the Extrusion Process

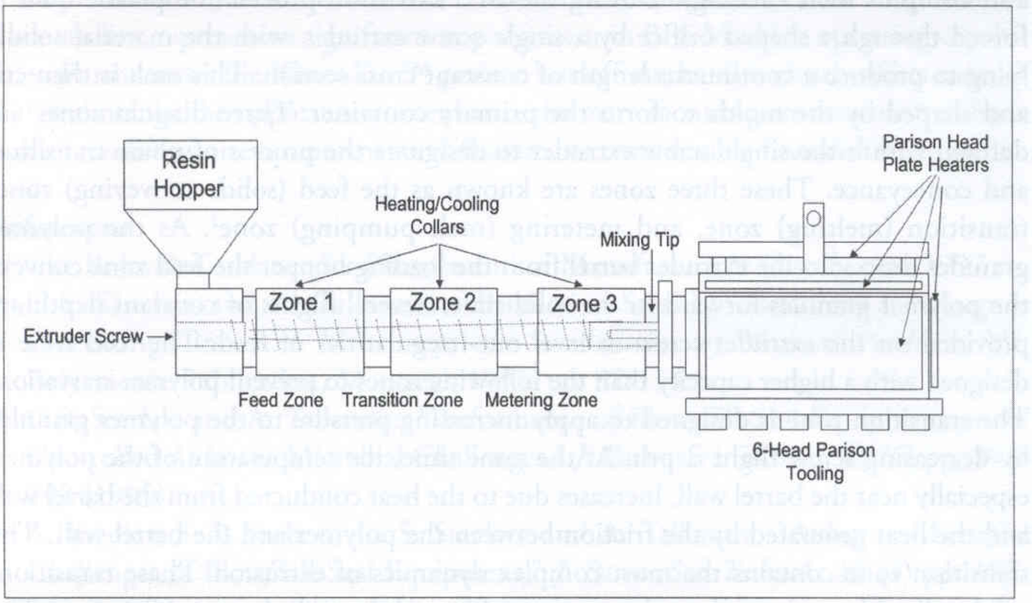
In BFS technology the extrusion process is a key step to convert polymer granules, using heat and pressure, into a useful homogenous liquid melt. Thermoplastic extrusion is a complex process that involves temperature, pressure, phase transition, and complex melt rheology. During the BFS extrusion process the plastic melt is forced through a shaped orifice by a single screw extruder, with the material solidifying to produce a continuous length of constant cross section. This melt is then cut and shaped by the molds to form the primary container. Three distinct zones are defined within the single screw extruder to designate the process of phase transition and conveyance. These three zones are known as the feed (solids conveying) zone, transition (melting) zone, and metering (melt pumping) zone[2]. As the polymer granules drop into the extruder barrel from the loading hopper the feed zone conveys the polymer granules forward in the solid state. Several flights of constant depth are provided on the extruder screw to level out irregularities of feed. The feed zone is designed with a higher capacity than the following zones to prevent polymer starvation. The transition zone is designed to apply increasing pressure to the polymer granules by decreasing screw flight depth. At the same time, the temperature of the polymer, especially near the barrel wall, increases due to the heat conducted from the barrel wall and the heat generated by the friction between the polymer and the barrel wall. The transition zone contains the most complex dynamics of extrusion. Phase transition, solid to liquid, occurs as the polymer moves forward through the transition zone. The transition is defined as solid bed reduction, a phenomenon in which there is a gradual depletion of polymer granules in subsequent screw flights[3]. The metering zone controls the uniformity of the output melt flow; a mixing tip installed on the ALP extruder screw enhances melt uniformity by providing intimate mixing of the various melt layers. Following the metering zone the melt passes into the parison tooling which is used to dictate the tubular shape of the extrudate.

On the ALP Model 624 BFS Machine electrical heating and water cooling is supplied to the extruder barrel by three cylindrical collars. Electrical heating is also supplied to plates installed on the exterior of the parison tooling. The plates on the parison tooling are not equipped with water cooling and rely on air conduction for transfer of heat energy. Each of the cylindrical collars and the side plates on the parison tooling are monitored for temperature by a thermocouple. Each thermocouple is identified by the BFS Machine Programmable Logic Controller (PLC) by location (Zones 1-3, Head 1-2). Temperature set points may be adjusted by the operator to process different types of polymer, such as polypropylene or high and low density polyethylene. The heaters are primarily used during cold extruder start-up to melt plastic remaining from the previous operation. Once the extruder zones reach set temperatures the heaters are rarely utilized to add additional heat. The frictional heat created by the mechanical action of the screw, counteracted by the cooling water, is normally sufficient to maintain temperature. This heating/cooling ability allows for operation of the extruder under a controlled set of parameters. Another critical parameter of the extruder is the L/D (Length/Diameter) ratio of the extruder screw which is defined as the length of the flighted portion of the screw divided by the inside diameter of the barrel. The ALP Model 624 is equipped with a screw with an L/D ratio of 24:1. This L/D ratio is common for both polypropylene and polyethylene extrusion. Figure 1 illustrates the extruder system installed on the ALP Model 624 B/F/S Machine.

Materials and Methods

An ALP Model 624 BFS Machine was used for the challenge study. The machine has a twenty-four cavity mold with a 2.1 cm^3 fill volume; the electronic fill system is located within the protection of a grade A (Class 100) air shower. The Blow-Fill-Seal Machine was set-up according to company procedure for process simulation (medium fill) testing. Product contacting surfaces were sterilized in-place with clean steam. Two hydrophilic sterilizing grade filters (nominal pore size 0.2 mm) were installed in

Figure 1: ALP Model 624 BFS Machine Single Screw Extruder



series upstream of the fill system. These filters were integrity tested both prior to and following use. A fill volume of 2 cm^3 was set and tryptic soy broth used as the filling medium. The rate of machine operation was set to produce 24 ampules per 11 seconds. The extruder and parison tooling temperatures and extruder screw rotational speed were maintained at routine set points throughout each fill study (155 to 165°C and 62 - 65 rpm respectively).

Four batches of spore contaminated low density polyethylene (Rexene 6010) were prepared separately, employing spores of *Bacillus subtilis* var. *niger* (ATCC 9372), by Air Dispersions Limited. *Bacillus subtilis* var. *niger* (ATCC 9372) is recommended by both the USP and EP for preparation of biological indicators for dry heat sterilization and also was used as the test organism in previous extruder studies[1]. Each batch of spore contaminated polymer was prepared through deposition of discrete air-dispersed spores on all surfaces of polymer granules using purpose-built equipment. The method of spore deposition ensured uniform distribution of spores on polymer granules. Spore population on the batches ranged from 9.9 x 10^3 to 2.0 x 10^6. Measurements of dry heat resistance were carried out, under standardized conditions, on test spores located on individual polymer granules. Batch spore population and D-values, derived at 160°C, are summarized in Table 1.

Extruder Challenge Results

For each batch of spore contaminated polymer (minimum of 35 kg), a separate medium fill study was carried out. Broth filled ampules were incubated for a minimum of 14 days at 20-25°C and 30-35°C, approximately half the units at each temperature range, so that the individual units could be inspected for appearance of visible microbial growth. The overall challenge characteristics and results are summarized in Table 1. Spore contamination of processed ampules was observed for each of the four spore contaminated polymer batches. The frequency of spore contamination ranged from

Table 1: Spore Polymer Challenge Characteristics and Results

Run	Mean Spore Challenge Level (spores/g)	D-Value	Number Filled	Number Positive	Fraction Contamination Level
ADL/9	4.5 x 10^5	1.22 min	11,256	15	1.2 x 10^{-3}
ADL/11	2.0 x 10^6	1.51 min	9,024	30	3.3 x 10^{-3}
ADL/12	9.6 x 10^5	2.01 min	7,656	108	1.4 x 10^{-2}
ADL/13	9.9 x 10^3	2.47 min	9,216	1	1.1 x 10^{-4}

1.2×10^{-3} to 1.4×10^{-2} for spore polymer batches ADL/9 and ADL/12 respectively; this twelve fold variation in frequency of contamination corresponds to a 1.6 fold change in D-value at 160° C. As in the previous study1, the frequency of ampule contamination is observed to increase with decreasing heat resistance. All positive ampules were examined by Air Dispersions Ltd. and confirmed to be the challenge test organism.

Discussion

Frequency of ampule contamination appears to be dependent on the dry heat resistance of the test spore and on the challenge level of test spores. Figure 2 is a plot, on semi-logarithmic scales, of the fraction of product contaminated against the measured D-value for each of the three batches with the nominal challenge level of around 10^6 spores/gram polymer. A direct relationship is evident with fraction of product contaminated increasing with increasing D-value.

Furthermore, a relationship was also evidenced between frequency of ampule contamination and parison position. The machine set-up utilized in this study uses

Figure 2: Fraction of Product Contaminated as a Function of the D-value

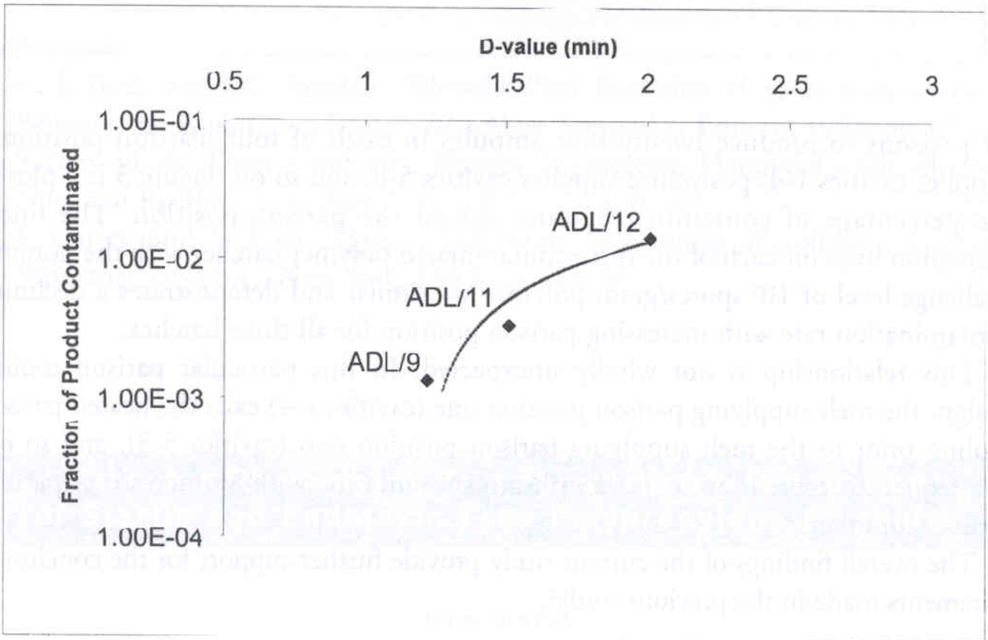


Figure 3: Percent of Contaminated Units per Parison Position

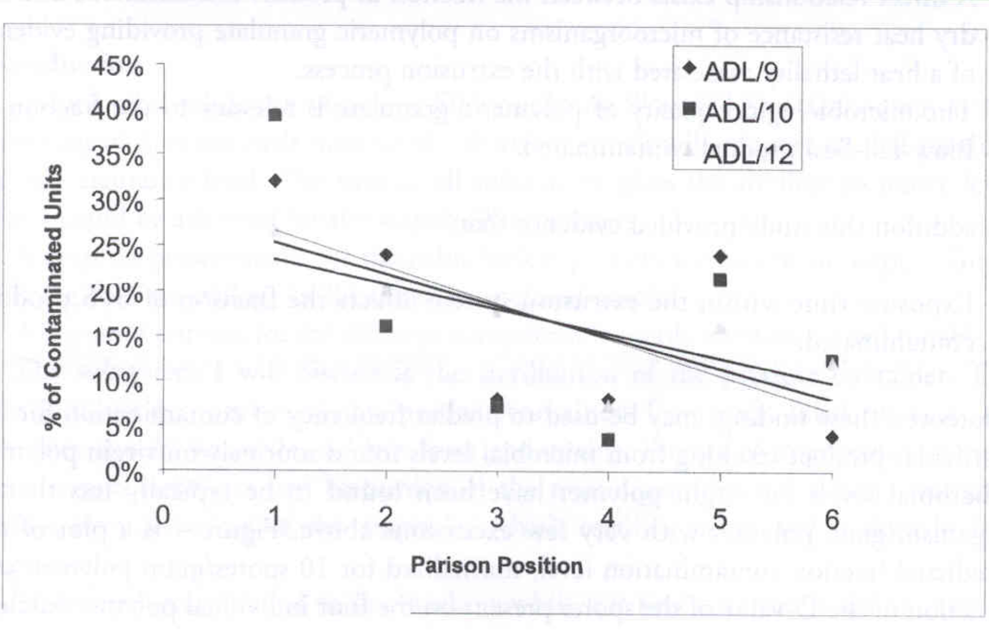
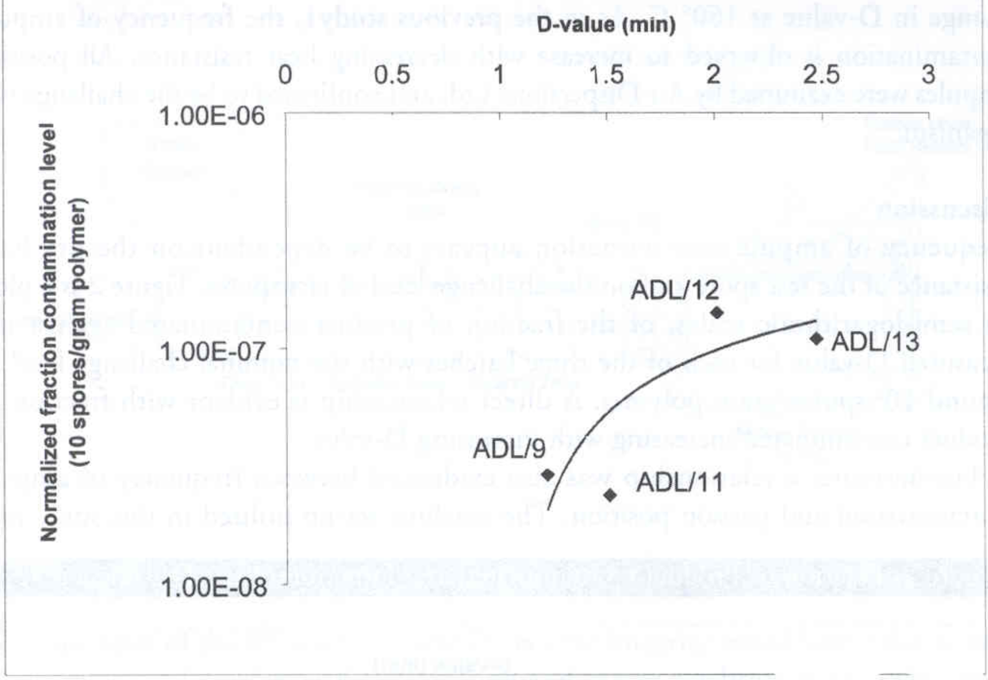


Figure 4: Normalized Fraction Contamination Level (10 spores/gram polymer)



six parisons to produce twenty-four ampules in cards of four. Parison position 1 supplies cavities 1-4, position 2 supplies cavities 5-8, and so on. Figure 3 is a plot of the percentage of contaminated units against the parison position. The linear regression lines for each of the three contaminated polymer batches with the nominal challenge level of 10^6 spores/gram polymer are similar and demonstrates a declining contamination rate with increasing parison position for all three batches.

This relationship is not wholly unexpected. In this particular parison tooling design, the melt supplying parison position one (cavities 1-4) exits the heated parison tooling prior to the melt supplying parison position two (cavities 5-8), and so on. Consequently, there is an increase in heat exposure time with an increase in parison position number.

The overall findings of the current study provide further support for the conclusion statements made in the previous study[1].

- Spores on polymeric granulate are inactivated by extrusion.
- A direct relationship exists between the fraction of product contaminated and the dry heat resistance of microorganisms on polymeric granulate providing evidence of a heat lethality associated with the extrusion process.
- The microbiological quality of polymeric granulate is relevant to the fraction of Blow-Fill-Seal product contaminated.

In addition this study provided evidence that:

- Exposure time within the extrusion system affects the fraction of BFS product contaminated.

Moreover, these findings may be used to predict frequency of contamination for the particular product resulting from microbial levels found routinely on virgin polymer. Microbial levels on virgin polymer have been found to be typically less than 1 organism/gram polymer with very few excursions above. Figure 4 is a plot of the predicted fraction contamination level, normalized for 10 spores/gram polymer, as a function of the D-value of the spores present on the four individual polymer batches.

The four datum points for spore polymer batches ADL/9, ADL/11, ADL/12, and ADL/13 are seen to fall around a common relationship.

Based upon this relationship, a polymer lot possessing a high bioburden level of 10 organisms/gram polymer and a high dry heat resistance with a D-value of 2 minutes, the predicted frequency of product contamination is 1.3 x 10^{-7} (i.e. 1 in around 7,500,000 items produced). This predicted frequency of product contamination is low and acceptable.

It is important to note that these findings and interpretations apply only to the specific conditions of this study. The influence of extruder design and the variables associated with operation of BFS machinery have not been determined at this time. Although thermoplastic extruders utilized for BFS technology are not currently designed to effect sterilization they posses inherent dynamic properties which allow for significant bioburden reduction through heat lethality and polymer encapsulation. Continued study of extruder performance, namely in the areas of container design, polymer type, and extruder operating conditions may allow for development of a model to predict microbial quality of BFS extruded containers. Furthermore, this information may in time be used to enhance extruder design and establish validated extruder operating parameters.

References:

1 C. J. Birch and C.S. Sinclair, "Blow/Fill/Seal Extrusion of Spore Contaminated Polymer: An Exploratory Study," *BFS News*, September Edition, 1998, pp. 13 -18.

2 Society of the Plastics Industry, Plastics Engineering Handbook, 4th ed. (Van Nostrand Reinhold Co., New York, 1976), pp. 160-162.

3 J. Carley and S. Levy, Plastics Extrusion Technology Handbook, 2nd ed., Industrial Press Inc., New York, 1989), pp. 24-28.