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Design of Experiment Approach to determine the effects of Tinuvin 622, recycling and sterilization by γ- irradiation on a medical polypropylene copolymer

https://doi.org/10.1515/cdbme-2025-0107

Abstract: Plastics are crucial in modern medical technology due to their adaptability and cost-effectiveness, but they also produce substantial waste. This study investigates the effects of recycling and γ-irradiation on stabilized polypropylene copolymer (PP) containing the secondary antioxidant Irgafos 168 (I168), the acid scavenger calcium stearate (CaSt), and the radiation stabilizer Tinuvin 622 (T622). Using a Design of Experiment (DoE) approach, it evaluates how processing, irradiation, and radiation stabilization interact, focusing on I168 degradation and rheological changes. When comparing the first and the third processing and γ-irradiation cycle, the I168 content and the formation of the radiolysis product 1,3-di-tert-butylbenzene (DTBB) were measured by high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC/MS). γ-Irradiation significantly reduced I168 content and lowered the viscosity of the PP. Although T622 mitigated effects, it didn't fully prevent I168 degradation. Processing influences were less significant compared to ionizing radiation. The study highlights the necessity for radiation stabilization during sterilization and suggests adjusting I168 post-irradiation for recycling. Continuous monitoring of degradation products is recommended to maintain product safety thresholds.

Keywords: γ-radiation sterilization, recycling, Design of Experiment (DoE), polymer additives

1 Introduction

The use of disposable items and sterilization methods have drastically reduced the probability of infection. However, these benefits have the disadvantage of the high volumes of plastic waste generated. In addition to the contaminated polymeric biomaterial waste, large quantities of non-infected plastic waste are produced. The majority of both is put to incineration, while mechanical recycling could be possibly considered especially for non-contaminated waste. [1] In order to protect the polymeric materials against thermal oxidation, e.g. during processing, or against the influence of ionizing radiation, which is used for sterilization purposes, additives are used [2]. The influence of recycling and irradiation of stabilized polyolefins, frequently used in sterile- barrier systems for polymeric biomaterials or in the medical application itself, e. g. syringes, has already been investigated in literature. G. Demertzis et al analyzed the radiation effect on plastic packaging films. Resulting from tris(2,4-di-tert-butylphenyl)phosphite (I168), which is one of the most widely used thermal stabilizers, the radiolysis product 1,3-di-tert-butylbenzene (DTBB) was identified [3]. L. Coulier et al. studied the influence of multiple recycling on Polyethylene and Polypropylene (PP) in terms of food safety. They identified, among other things, DTBB as a degradation product of I168 [4]. Previous analyzes did not reveal any health risk for the degradation product mentioned [5,6]. The study presented in this report differs from previous findings in the literature in considering the influence of processing and irradiation combined and thus looking at recycling in medical technology, taking sterilization into account. In addition to the manufacturing-related influences on a medical device, the influence of radiation stabilization was also evaluated.

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2 Materials and Methods

2.1 Material

An isotactic polypropylene copolymer containing < 10mol% ethylene units in additive free powder form provided by Borealis (Burghausen, Germany) was analyzed. The T622-free resin was compounded with 0.05 wt.% calcium stearate (CaSt) and 0.15 wt.% Irgafos 168 (I168) using a ZE28 x 44D –BP-UG extruder (KraussMaffei Group GmbH, Parsdorf, Germany). Depending on the sample, 0.18 wt.% of Tinuvin 622 (T622) was added. The additives were provided by BASF Schweiz AG (Kaisten, Switzerland).

2.2 Design of Experiment

The Design of Experiment approach (DoE) is a type of statistical experimental design model that enables the statistical analysis of various influencing factors, hereinafter referred to as main factors, on defined responses. In this study, a full factorial experimental design was chosen to be able to evaluate all interactions. In Table 1 the main factors are shown in the coded form. The responses considered were the content of I168, the formation DTBB and the zero viscosity.

Table 1: Assignment of influencing variables in coded form.

	Influencing Factors in coded form	**-1**	**1**
A	*Processing Cycle*	1	3
B	*Irradiation [kGy]*	0	25
C	*Initial T622 Content [%]*	0	0.18

2.3 Sample Preparation

Tensile test specimens (Type 5A, DIN EN ISO 527-2-06) were produced via injection molding (Babyplast 6/10 P, Rambaldi srl, Italy). The polymer melt (31.3 mm stroke) was injected at 55 bar, with a 50 bar holding pressure and a cylinder temperature of 200 °C. Samples underwent three processing cycles. Some samples were subjected to γ-irradiation (25 kGy, 6 kGy/h) by BGS GmbH, Germany. All specimens were analyzed over four weeks post-processing and/ or irradiation to minimize aging effects.

2.4 Chromatography

To measure the I168 content using HPLC analysis 2 g of the sample cut into pieces of 2x2x2 mm were dissolved in boiling toluene (20 ml, 115 °C, 45 min) under reflux. After dissolution, 25 mL methanol was added to precipitate PP, leaving I168 in solution. The extract was diluted to 50 mL with a 1:1 methanol-toluene mixture, filtered, and further diluted (1:1 methanol). HPLC analysis (Agilent 1260, DAD detector) was performed using a 125 mm C18 column. A gradient of two mobile phases (A: methanol/water 80:20; B: ethyl acetate/acetonitrile 50:50) was applied over 12 min, followed by 5 min at 100% phase B. The flow rate was 0.8 mL/min, column temperature 25 °C, and detection at 272 nm. Quantification was based on an external standard calibration with I168 (Merck KGaA) in toluene/methanol (1:1), covering 6–42 µg/mL, corresponding to 0.016–0.1 wt.-% in the sample [7]. To measure the DTBB content using GC/MS analysis 2 g of the cut sample was extracted using 50 mL of chloroform in a soxhlet extractor. The extraction was carried out at 115°C for a period of 4 hours. After the extraction, the extract was filtered. The extracts were analyzed using a Clarus 600/SQ8 GC/MS Spectrometer (GC/MS) (PerkinElmer, Waltham, United States). The oven was heated to 50°C for 5 min and then heated to 320°C at 10 K/min. The temperature was held for 13 min. The measurement was carried out splitless under a carrier gas flow of 1.2 mL/min helium. To identify the radiolysis product DTBB, the masses 175 and 190 were measured in the selected ion monitoring mode (SIR). Quantification was carried out using an external standard with a concentration of 1 µg/mL.

2.5 Oscillation Rheometry

Oscillatory rheometry was performed using an ARES Rheometer (TA Instruments, Germany) in a plate-plate setup (25 mm diameter). Test specimens were heated to 180 °C and trimmed to a 1 mm gap. Measurements were conducted after 5 min at 180 °C in a frequency sweep (0.4-400rad/s defermation). An amplitude sweep was performed to confirm the linear viscoelastic (LVE) range. The zero viscosity was the calculated complex viscosity at a frequency of 0.1 rad/s.

2.6 Statistics

Graphical representation was performed using OriginPro (OriginLab Corporation). Significant differences were identified using one-way ANOVA (significance level ≤ 0.05, Tukey test). Design-Expert (Stat-Ease, Inc., Minneapolis, USA) was used for DoE evaluation. R^2 values represent the statistical outcomes.

3 Results and Discussion

The standardized effect of the main factors and their interactions on the response of the I168 component is shown in Figure 1.

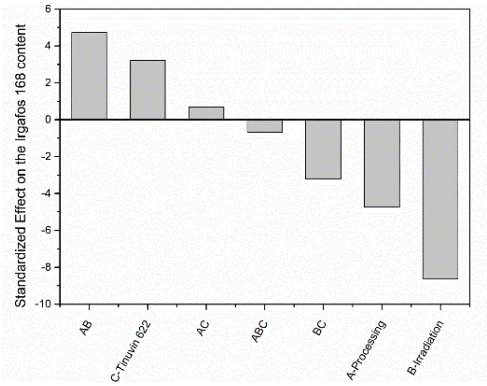

Figure 1: Illustration of the standardized effect of the main factors and their interactions on the degradation of I168

This representation is also referred to as a Pareto chart and is a result of the DoE evaluation. The greatest measurable effects were caused by the interaction of irradiation and processing.

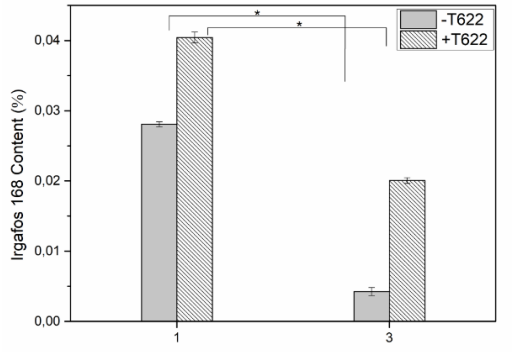

Figure 2: Mean and standard deviation of the I168 content as a function of the main factor processing without the irradiation influence. The asterisks mark a significant change in n= 3 measurements

Figure 2 shows the I168 content in % as a function of the processing (Cycle 1 ↔ Cycle 3). The solid bars show the results of the T622-free PP, the hatched bars those of the stabilized PP. The starting concentration in cycle 1 was well below the added level of 0.15% of I168 for both compounds. The stabilizing effect of the additive during compounding led to less I168 consumption when T622 was present. After three processing cycles, the additive's concentration dropped significantly, regardless of Tinuvin 622. In T622-free PP, I168 decreased by 85%, while in radiation-stabilized PP, it only fell by 50%, indicating that T622 protected the compound from processing. However, after irradiation, I168 levels in all samples were below the quantification limit of 0.007%, showing that T622 cannot adequately protect I168 when exposed to radiation. Figure 3 shows the concentration of the DTBB as a function of the cycle for the irradiated samples. Since DTTB is the product of radiolysis of I168, the unirradiated samples are not shown.

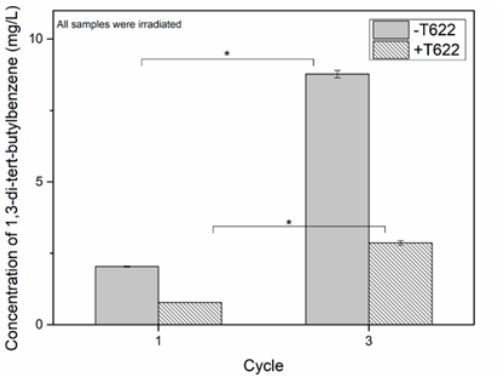

Figure 3: Concentration of the DTBB in mg/L depending on the processing cycle. The samples considered were irradiated. The asterisks mark a significant change in n= 3 measurements.

The formation of the degradation product is considered depending on the presence of the radiation stabilizer. Even after the first processing and irradiation, less of the radiolysis product was formed in the radiation-stabilized PP compared to the sample T622-free. This effect increased significantly after cycle 3. The T622 supported the antioxidant in stabilizing the polymer which resulted in less degradation. The degradation of the additives and the polymer resulted in changes in the material properties. The degradation of the additives and the polymer resulted in changes in the material propertyes. Zero viscosity was selected as the sensitive parameter for evaluating material degradation.

The zero viscosity correlates with the molar mass of the polymer and is therefore a good comparative value [8]. Figure

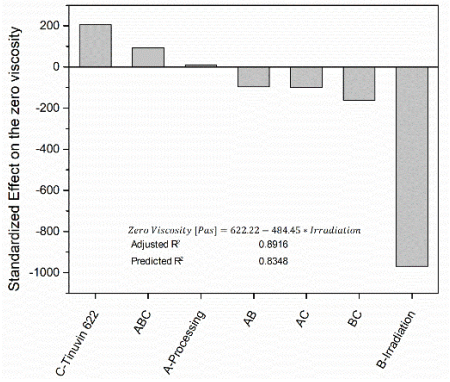

Figure 4: Illustration of the standardized effect of the main factors and their interactions on the zero viscosity. Indication of the prediction model and the statistical characteristics of the Anova.

4 shows the Pareto chart of zero viscosity. The influence of irradiation exceeded the influence of all other main factors and interactions by at least approx. 80%. This clear effect was used to generate the prediction model shown in Figure 4. The statistical results provide a significant model with a prediction probability of 83%. Sterilization had the greatest influence on the material property of zero viscosity and, as a result, on the molar mass. The ionizing radiation resulted in a significant chain shortening.

4 Conclusion

It can be concluded that sterilization had a significant influence on the materials tested. In addition to the significant reduction in the content of I168 and the increased formation of the degradation product, this main factor resulted in a significant reduction in the zero viscosity and the associated molar mass. The influence of processing was small compared to the influence of irradiation, in particular for the zero viscosity. The change in molar mass can result in processing problems and changes in other material properties, which need to be analyzed further. The T622 stabilized the polymer in addition to the basic stabilizer. It was observed that the presence of radiation stabilizer kept the content of I168 on a higher level over the measured cycles. Under the influence of irradiation, however, the degradation of the content of I168 could not be suppressed. The reduced formation of the radiolysis product DTBB under the presence of T622 showed that T622 had a stabilizing effect, which nevertheless does not ensure the preservation of the content of I168 via irradiation.

To ensure stable processing and consistent properties of the medical device, radiation stabilization is strongly recommended for planned sterilization with ionizing radiation. Based on the results, the secondary antioxidant I168 should be adjusted after irradiation if recycling is planned. The formation of the investigated degradation product is harmless according to the current state of scientific knowledge [5,6]. In the case of recycling-related accumulation, however, the permissible concentration of the application should be checked.

Author Statement

Research funding: The author state no funding involved. Conflict of interest: Authors state no conflict of interest. We would like to thank Borealis Polymere GmbH for providing the materials and BGS Beta-Gamma-Service GmbH & Co. KG for the irradiation of the samples.

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