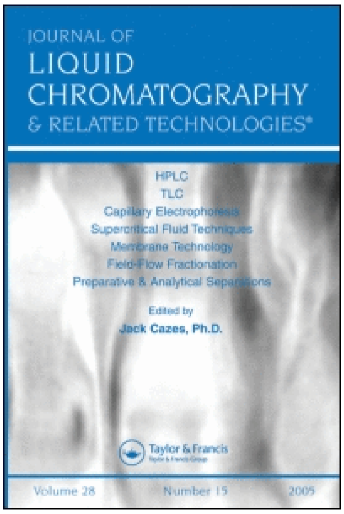

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RAPID IDENTIFICATION OF ANTIOXIDANTS IN PHARMACEUTICAL PACKAGINGS WITH PLANAR CHROMATOGRAPHY COUPLED WITH PHOTODENSITOMETRIC DETECTION

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ABSTRACT

A rapid assay was developed on the RP HPTLC C_{18} bonded silicagel with a ternary mobile phase constituted of (acetonitrile : methanol : tetrahydrofuran, 50 : 25 : 25 v/v/v) to separate polypropylene additives. The detection was performed by photodensitometry at a UV wavelength of 200 nm and 280 nm also after a derivatization with the phosphomolybdic acid at 520 nm. The technique was applied to identify phenolic and phosphitic antioxidants extracted from polypropylene by the dissolution-precipitation method.

INTRODUCTION

The additives used for polyolefines in medecine, pharmacy,[1] and food packaging[2] have mostly been studied by liquid chromatography. They belong to several chemical classes (phenolic, organic phosphites, sulfuric as antioxidants, and amides as lubricating or antistatic agents). They exhibit a wide range of molecular weights, in polarity, in solvent solubility, and in volatility.[3] Also, the experimental conditions necessary to prevent additive degradation such as extraction parameters (solvent, temperature, and duration) are difficult to define.[4] All these factors lead to several practical problems for developing only one chromatographic method to analyse the plastic additives. High performance liquid chromatography (HPLC) coupled with different detections: UV, electrochemistry, light scattering,[5] and mass spectrometry[6] are important techniques for qualitative and quantitative analysis of polymer additives. Thin layer chromatography (TLC) attracts attention, especially as this may be useful as a scouting technique before the switching to HPLC to identify the formulations of plastics which are usually not divulged by manufacturers. TLC was developed generally on silicagel with appropriate eluents and spray reagents.[7,8,9,10] Otherwise, in a recent study,[11] planar chromatography showed an interesting potential for determination of migrating impurities into pharmaceutical materials. The work described in this paper proposes separation and identification of polyolefine additives listed in the European Pharmacopeia except (1,3:2,4)bis-(3,4-dimethylbenzylidene)sorbitol and the 2,4-di-tert-butyl phenol used in food packaging (Table 1).

The main differences between our study and others, are the stationary phase (reversed-phase C_{18} bonded silicagel) and the post chromatographic derivatization with ethanolic solution of phosphomolybdic acid[12] using a Derivapress apparatus to give homogeneous derivatization.[13]

EXPERIMENTAL

Apparatus

Three µL of the following standard additives (Table 1):Weston 618, PS 802, PS 800, Hostanox SE 10, Irganox 1076, Phosphite ester, oxidized phosphite ester, Irganox 1330, Irganox 1010, BHT, BHA, Hostanox 03, and 6 µL of 1,3,2,4-p-methyl-benzylidene sorbitol and oleamide were automatically streaked on RP-HP-TLC plates without a fluorescence indicator, 10 cm x 10 cm, Merck, (Nogent-sur-Marne, France).

The post chromatographic derivatization step was performed with an ethanolic solution of phosphomolybdic acid reagent,[12] by the over pressured derivatization technique,[13] using a Derivapress, AR 2i, (Clamart, France). This technique implies the use of polymer foam which is first impregnated with the reagent, and secondly applied under pressure on the plate. The physical properties of the foam allow for the reabsorption of the excess of reagent when the pressure is released.

The chromatograms were recorded by a photodensitometer model CD - 60, Desaga, (Heidelberg, Germany) at a wavelength of 200 nm and 280 nm (before derivatization) and 520 nm (after derivatization).

Reagents and Chemicals

The standard additives were obtained commercially from different manufacturers (Table 1), the phosphomolybdic acid reagent was provided by Merck (Nogent-sur-Marne, France). The solvents used, were HPLC grade. Methanol and acetonitrile provided by Prolabo (Fontenay-sous bois, France) and tetrahydrofuran not stabilized by Osi (Elancourt, France).

Preparation of Sample and Standards Solutions

The standards were dissolved in tetrahydrofuran in order to obtain a concentration of 1 mg/mL for Weston 618, PS 802, PS 800, Hostanox SE 10, Irganox 1076, Phosphite ester, Oxidized phosphite ester, Irganox 1330, Irganox 1010, BHT, 2,4-di-tert-butyl phenol, Hostanox 03, and 2 mg/mL for (1,3:2,4)bis-(3,4-dimethylbenzylidene)sorbitol and oleamide. A mixture of seven additives with no interference had the composition: phosphite ester, oxidized phosphite ester, Irganox 1330, Irganox 1010, BHT, Hostanox 03, and 1,3,2,4-p-methyl-benzylidene sorbitol, was weighed at 1mg/mL for two tests.

The first test was the automatic streaking of 3 μL to derivatize after the run with phosphomolybdic acid. However, the second is the respective parallel run of mixture (3μL) and of polypropylene extract (8 μL) on the same plate. Additives were extracted from polypropylene by dissolution - precipitation procedure. For this, 1 g of polypropylene was dissolved in 20 mL of refluxing toluene under 30 mins of magnetic stirring. The polymer was precipitated by 150 mL of methanol then filtrated on glass fibre superimposed to a whatman 0.45 μm porosity, 47 mm diameter type GF/C filter. The extract was evaporated to dryness by rotary evaporation. Then, the residue was dissolved in 1 mL of tetrahydrofuran and an aliquot of 8 μL was streaked on the plate.

Table 1

Chart of Additives

Additives	Chemical Name	Supplier
BHT	2,6-Di-tert-butyl-4-methylphenol	Ciba-Geigy
Irganox 1330	1, 3, 5-trimethyl-2,4,6-tris (3, 5-di-tert-butyl-4-hydroxy-benzyl) benzene	Ciba-Geigy
Irganox 1010	Tetrakis methylene (3,5-di-tert-butyl-4-hydroxyhydro cinnamate)methane	Ciba-Geigy
Irganox 1076	Octadecyl-3-5-di--tert-butyl-4-hydroxyhydro cinnamate	Ciba-Geigy
Hostanox 03	Bis[3,3-bis[3-1,1-dimethylethyl)-4-hydroxyphenyl] butanoate]ethylene	Hoechst
Hostanox Se 10	Di-octadecyl-dissulfure	Hoechst
Ps 800	Dilaurylthiodiprop--ionate	Ciba-Geigy
Ps 802	Di-stearyl-thiodipropionate	Ciba-Geigy
Weston 618	Di-stearyl-penta-erythritol-di-phosphite	Ciba-Geigy
Irgafos 168	Tris(2,4-di-tert-butylphenyl) phosphite	Ciba-Geigy
Oxidised Irgafos 168	Tris(2,4-di-tert-butylphenyl) phosphate	Ciba-Geigy
Oleamide	9-Octadecenamide	Croda Universal Ltd
DBS	(1,3:2,4)-bis-(3,4-dimethyl-benzyl)sorbitol	Milliken Chemical
BHA	tert-butyl hydroxy anizole	Merck

Planar Chromatography

Aliquots (μL) of samples, standards, and mixture solutions were applied on the RP-HPTLC, plate at 1.5 cm from the lower edge. The eluent was: acetonitrile, methanol, tetrahydrofuran (50 : 25 : 25, v/v/v). The chromatograms were developed in a saturated atmosphere tank and the solvent front migrated 8 cm above the application line. The running time was 15 min.

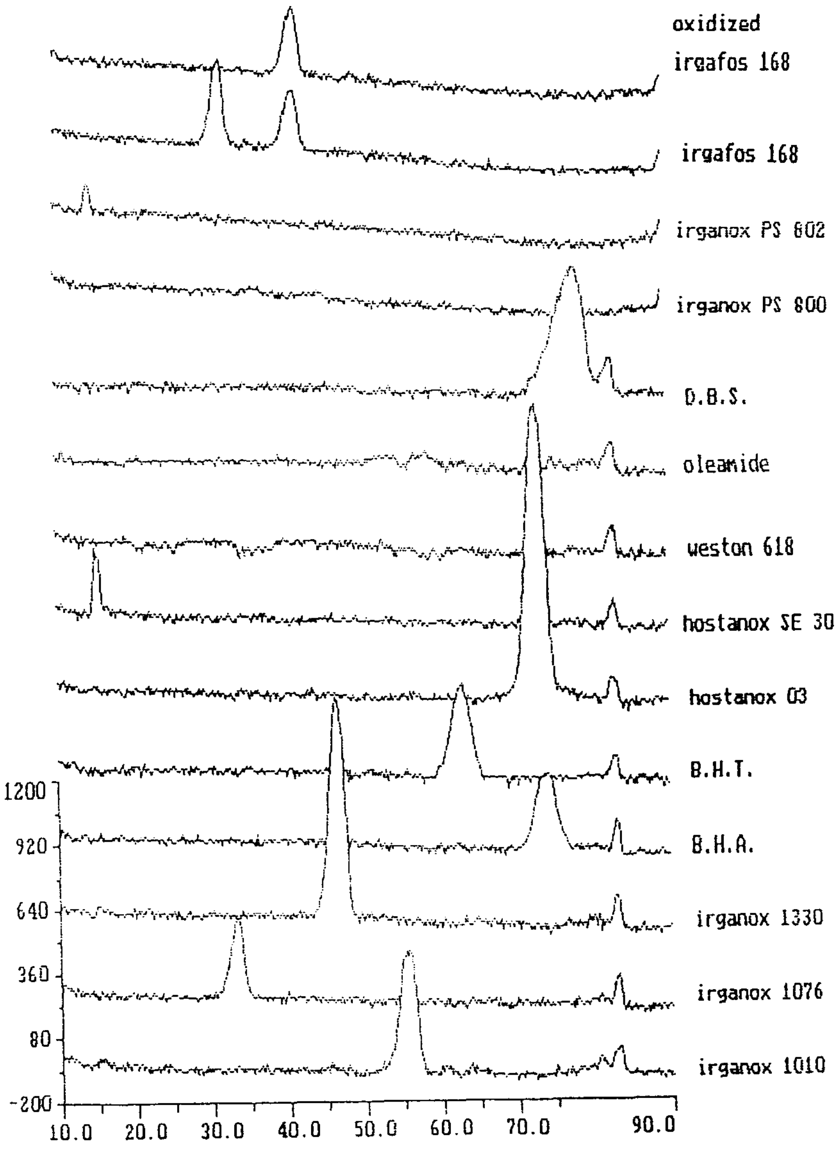

Figure 1. Separation of ten additives on RP HPTLC C18. Eluent: acetonitrile, methanol, tetrahydrofuran, 50/25/25, v/v/v.

RESULTS AND DISCUSSION

Detection at 200 nm

All additives were detected at this wavelength except the Weston 618 and PS 800. The eluent makes the migration of ten additives (Figure 1) possible but discriminates two additives which are the PS 802 and the Hostanox SE 10. The two latter sulphuric antioxidants exhibit alkylated groups ($-C_{18}$ H37) inducing the adsorption on the stationary phase. All migrated additives give only one spot which means that there are no impurities related to the process of synthesis or degradation products. However the Irgafos 168 shows, in our experimental conditions, two spots. The minor spot caracterized by the largest migration corresponds to a derivated Irgafos 168 product. It exhibits the same migration such as the phosphate ester.

Many polyolefines contain phosphite antioxidants namely the Irgafos 168 (Table 1) and the tri-nonyl-phenyl phosphite. Their primary function is the ability to decompose hydroperoxides resulting from thermal degradation of polymers and involving scission chains. The tetrahydrofuran used was not stabilized with hydroquinone, necessary for prevention of excessive peroxide formation. We estimate that the oxidation of the Irgafos 168 by the peroxides at moderate temperature produces the phosphate ester.

Whereas the main spot of Irgafos 168 and the Irganox 1076 exhibit the lowest R_F value. Effectively the hydrophobic interaction between the C_{18} bonded silicagel and the six ter-butyl of Irgafos 168 and the alkylated chain of Irganox 1076 involves a lower migration. However the Hostanox 03 shows a R_F which is greater than the R_F of phenolic antioxidants. Effectively, its molecular structure exhibits four (-OH) which are not sterically crowded with the ter-butyl (position ortho, C 2) group in comparison with the other phenolic antioxidants which exhibit two tert-butyl groups (position ortho, C2 and C8). Polar interactions developed between the hydroxyl groups and the mobile phase induces the largest migration.

Detection at 280 nm

The oleamide and the phosphate ester are not detected at 280 nm (Figure 2). The linear structure of oleamide do not allow for any specific absorption. However the transoformation of the phosphite ester in to a phosphate involves an electronic delocalization inducing the decrease of phenol specific absorption.

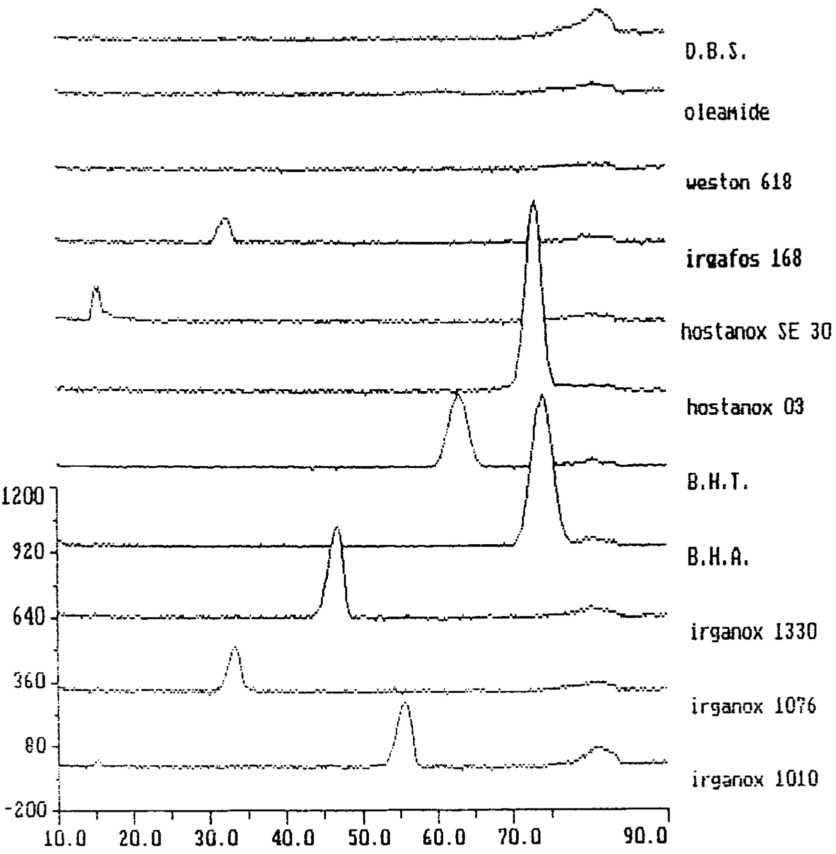

Figure 2. Separation of additives on RP HPTLC C18. Eluent: acetonitrile, methanol, tetrahydrofuran, 50/25/25, v/v/v. Detection at 280 nm.

Detection at 520 nm

Phosphomolybdic acid can oxidize a large number of organic substances and gives blue-violet coloured spots on a yellow background. The automatic streaking of a mixture containing eight additives which were separated to a greater degree in our experimental conditions (Figure 3) shows that only the BHT, the Irganox 1010, and the Irganox 1330 were visualised with phosphomolybdic acid.

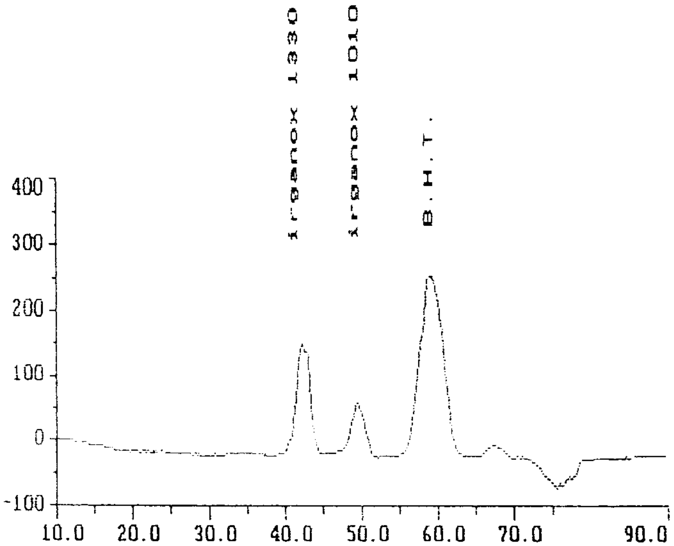

Figure 3. Separation of additives on RP HPTLC C18. Eluent: acetonitrile, methanol, tetrahydrofuran, 50/25/25, v/v/v. Over pressure derivatization with isopropanolic solution of phosphomolybdic acid. Detection at 520 nm.

Application

The detection at 200 nm, determined most additives without a noise background, as was expected. Also, their signal / noise was better at 200nm than at 280 nm and 520 nm.

The analysis of additives, extracted from polymeric matrix by dissolution-precipitation method, was only carried out at 200 nm.

Comparison between polypropylene extract and mixture additives (Figure 4) establishes that the polymer was stabilized by seven chemicals. Traces of the phosphate ester and the Irganox 1330 were identified.

The formulation of the polymer shows, also, the Irganox 1010, the Hostanox 03, and the DBS. We observed two unknown compounds with a respective migration distance of 67.5 and 80 mm above the application line.

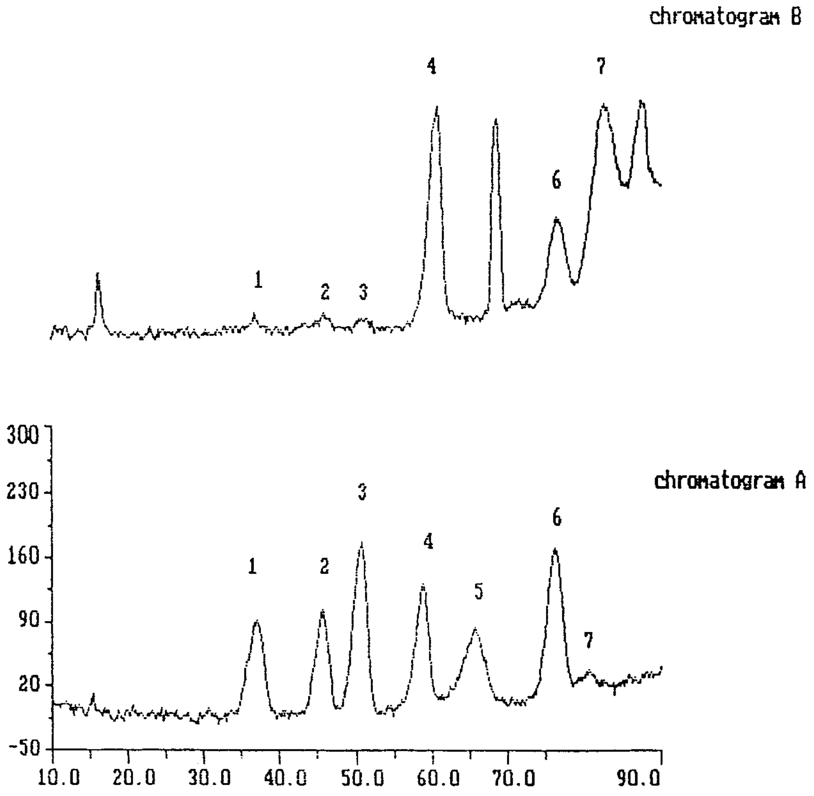

Figure 4. Separation of additives on RP HPTLC C18. Eluent: acetonitrile, methanol, tetrahydrofuran, 50/25/25, v/v/v. A: Chromatogram of mixture of standard additives. B: Chromatogram of polypropylene extract. Peaks: 1 Irgafos 168, 2 Oxidized Irgafos 168, 3 Irganox 1330, 4 Irganox 1010, 5 BHT, 6 Hostanox 03, 7 1,3,2,4-p-methyl-benzylidene sorbitol.

CONCLUSION

This proposed analytical method makes it possible to detect at 200 nm and to identify the additives which are characterized by a wide range in polarity (Table 1) with a short analysis time. Attention should be drawn to the degradation of the Irgafos 168 in tetrahydrofuran solution. The determination of additives in polymer is carried out generally with the reversed-phase bonded alkyl silicagel as stationary phase and with polar solvents (tetrahydrofuran, acetonitrile, methanol, water) as eluents.

We estimate that this analytical system is suitable for phenolic antioxidants. However, some experimental conditions may be optimized to avoid degradation of phosphite additives. Planar chromatography with multimode detection allows for separation or selective detection of many additives generally used in plastic material formulations and, therfore, confirms its interest in the field of content - container interaction studies.

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