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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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Re: Expediente No. **06.090.329**

Solicitud de patente a nombre de **SUN CHEMICAL CORPORATION**

Yo, DILIA RODRIGUEZ D'ALEMAN, identificada como aparece al pie de mi firma, domiciliada en la carrera 11 No. 86-53, piso 6, obrando como obrando como apoderada de la sociedad **SUN CHEMICAL CORPORATION**, domiciliada en New Jersey, Estados Unidos, solicitante de la patente de la referencia, interpongo recurso de reposición contra la resolución No. 9742 del día 28 de febrero de 2012, expedida por el Superintendente de Industria y Comercio, por medio de la cual se niega el privilegio de patente para la solicitud contenida en el expediente de la referencia.

1. FUNDAMENTOS DEL RECURSO

1.1 Mi mandante se permite manifestar a ese despacho que se reafirma en todos y cada uno de los argumentos que hacen parte integrante de la respuesta al oficio de fondo No. 4343 notificado por fijación en lista el día 26 de marzo de 2010, presentada ante ese despacho el 24 de junio de 2010; el oficio de fondo No. 11285, notificado por fijación en lista el día 3 de septiembre de 2010, presentada ante ese despacho el día 29 de diciembre de 2010; y el oficio de fondo No. 11534, notificado por fijación en lista el día 22 de julio de 2011, presentada ante ese despacho el día 27 de septiembre de 2011.

1.2 El indebido análisis del nivel inventivo

En primer lugar, en su resolución ese Despacho cita la anterioridad D2 que corresponde a un catálogo de producto publicado en el año 2007, mientras que la solicitud reivindica prioridad del 12 de Marzo de 2004, esto es, años antes a la publicación del documento D2 citado por el examinador.

En este sentido, se le recuerda al examinador que, de acuerdo a la Decisión 486 (tal como veremos más adelante), aquellos documentos publicados con posterioridad a la fecha de prioridad reclamada son aceptables para evaluar la novedad o la altura inventiva de una solicitud. En vista de lo anterior, para el solicitante resulta poco comprensible que ese Despacho insista en citar el mismo documento tanto en el oficio No. 11534 como en la presente resolución a sabiendas que el mismo no es aceptable a la luz de la legislación vigente, menos

aún cuando dicho Despacho en ningún momento se pronunció en contra de la prioridad reclamada por el solicitante.

Existe, por lo tanto, si bien no se está objetando por falta de novedad la presente solicitud, una indebida interpretación del artículo 16 de la Decisión 486 de la Comunidad Andina en tanto en el oficio No. 11534 como en la presente resolución en cuanto a lo que se debe considerar el estado del arte, toda vez que no se tuvo en cuenta la fecha de la prioridad reivindicada por la solicitud en estudio y, por lo tanto, se cita como dentro del estado de la técnica para la presente solicitud el documento D2.

Ante todo, tenemos que el artículo 16 establece lo siguiente:

“Una invención se considerará nueva cuando no está comprendida en el estado de la técnica.

El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida.

Sólo para el efecto de la determinación de la novedad, también se considerará dentro del estado de la técnica, el contenido de una solicitud de patente en trámite ante la oficina nacional competente, cuya fecha de presentación o de prioridad fuese anterior a la fecha de presentación o de prioridad de la solicitud de patente que se estuviese examinando, siempre que dicho contenido esté incluido en la solicitud de fecha anterior cuando ella se publique o hubiese transcurrido el plazo previsto en el artículo 40.”
(El subrayado es nuestro)

Adicional a lo anterior, además de la interpretación absolutamente errada del artículo 16, también se presenta la misma situación con relación al artículo 9 de la Decisión 486, puesto a que se obvia en su totalidad el concepto de prioridad que fue reclamada por el solicitante de la presente solicitud, puesto que su Despacho pasa por alto que, al aceptarse la reivindicación de prioridad, se tendrá como estado de la técnica únicamente aquella información que fue publicada o presentada antes de la fecha de prioridad reconocida.

A fin de demostrar la equivocación en la interpretación en que la Superintendencia de Industria y Comercio se encuentra nos permitimos citar el artículo 9 de la Decisión 486 el cual establece: *“La primera solicitud de patente de invención o de modelo de utilidad, o de registro de diseño industrial o de marca, válidamente presentada en otro País Miembro o ante una autoridad nacional, regional o internacional con la cual el País Miembro estuviese vinculado por algún tratado que establezca un derecho de*



prioridad análogo al que establece la presente Decisión, conferirá al solicitante o a su causahabiente un derecho de prioridad para solicitar en el País Miembro una patente o un registro respecto de la misma materia. El alcance y los efectos del derecho de prioridad serán los previstos en el Convenio de París para la protección de la Propiedad Industrial... (El subrayado es nuestro)

En vista de lo anterior, el documento D2 resulta improcedente y debe ser retirado de la Resolución. De igual forma, cualquier argumento basado en la combinación de las anterioridades D1 y D2 se torna irrelevante y carente de todo fundamento, por lo que es claro que ese Despacho ha efectuado un indebido análisis de la altura inventiva.

A pesar de lo anterior, el solicitante quisiera hacer los siguientes comentarios respecto a la anterioridad D1.

En su resolución, ese Despacho establece lo siguiente:

“Dado que la característica técnica y principal de la tinta para impresión offset, son los ésteres presentes en ella, se puede establecer que dichos compuestos ya habían sido revelados en las anterioridades D1 y D2; por lo que para una persona de nivel medio en el área técnica resulta evidente formular la tinta de la solicitud.”

Puesto que, como se establece arriba, la anterioridad D2 no puede ser tenida en cuenta por haber sido publicada de manera posterior a la fecha de prioridad reclamada, es necesario insistir como se ha hecho en repetidas oportunidades que la anterioridad D1 no enseña ni sugiere ácidos carboxílicos con más de 2 grupos de ácido carboxílico y mucho menos ésteres que emplean dichos ácidos.

De hecho, como el examinador podrá notar, la anterioridad D1 enseña en el resumen y el párrafo [0013] tintas para impresión offset que comprenden un solvente que contiene un **diester** de un ácido alifático dibásico. De hecho, la anterioridad D1 enseña un compuesto diester formado al reaccionar un di-ácido con un alcohol bi-funcional tal como 1,3-pantandiol. Esta reacción, como bien lo sabe el experto con habilidad ordinaria en la materia, lleva a la formación de poliésteres los cuales **no corresponden** a los ésteres policarboxílicos reclamados en la presente solicitud, los cuales son el producto de la reacción de un ácido policarboxílico y un alcohol monohídrico.

D1 también enseña un barniz para impresión offset que contiene monoésteres de ácidos grasos. Los monoésteres de ácidos grasos **no incluyen** un ester de de un ácido policarboxílico que tiene más de dos (2) grupos de ácido carboxílico con un alcohol monohídrico que tiene al menos 4 átomos de carbono.



Por lo tanto, D1 no enseña ni sugiere una tinta o barniz que contiene un solvente que incluye un solvente que contiene ésteres de ácidos tribásicos o superiores, y ciertamente no enseña ni sugiere un “éster de un ácido policarboxílico que contiene más de 2 grupos de ácido carboxílico con un alcohol monhídrico que tiene al menos 4 átomos de carbono” como se recita en la reivindicación 1.

Los argumentos del examinador dejan entrever un estudio retrospectivo de la solicitud ya que el simple hecho de saber que los ésteres de ácidos cítricos ya eran conocidos en el arte y se encontraban disponibles comercialmente al momento de presentar la solicitud, no es argumento suficiente para demostrar que era obvio para el experto con habilidad ordinaria en la materia reemplazar un solvente en una tinta para impresión offset con un éster de ácido cítrico comercialmente disponible. Debe existir algún tipo de sugerencia o enseñanza en el estado del arte que lleve al experto con habilidad media en la materia a hacer lo que el solicitante ha hecho con el fin de declarar que las reivindicaciones son obvias y destruir la altura inventiva de la solicitud. A la luz de los argumentos anteriores, es claro que ese Despacho no ha proporcionado argumentos suficientes que permitan demostrar que el arte previo enseña, sugiere o motiva al experto con habilidad ordinaria en la materia a producir una tinta o barniz para impresión offset como el que se reclama.

Como si lo anterior no fuera suficiente, el solicitante anexa un documento titulado “The plasticizer market: an assessment of traditional plasticizers and research trends to meet new challenges” de Mustafizur Rahman y Christopher S. Brazel, en el cual se demuestra que al momento del desarrollo de la presente solicitud los ésteres de ácido cítrico eran conocidos como plastificantes funcionales en la producción de plásticos. Por ejemplo, en la página 1227 se enseña el desarrollo de nuevos plastificantes para reemplazar plastificantes tradicionales, entre los nuevos plastificantes se encuentran los ésteres de ácido cítrico, aceite de soya epoxidado, polímeros de injerto de PVC/EVA y terpolímeros y que “hay disponible una plétora de plastificantes para escoger, dependiendo de los requerimientos de procesabilidad y uso final”.

La anterioridad D1 no enseña ni sugiere incluir un plastificante en una tinta o barniz de impresión offset, no proporciona motivación alguna para hacerlo. La anterioridad D1 tampoco provee una guía para escoger específicamente los ésteres de ácido cítrico de entre la “plétora de plastificantes” conocidos y disponibles a la fecha de la presentación de la solicitud. Más aún, la anterioridad D1 no enseña o sugiere seleccionar un éster de un ácido policarboxílico que sea insoluble en agua. Además de lo anterior, los ésteres de ácido cítrico son conocidos por presentar varios inconvenientes; por ejemplo, en la página 1229 del documento anexo se enseña que los ésteres de ácido cítrico son relativamente

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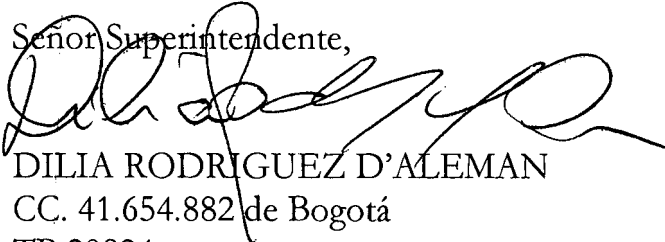
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volátiles y sensibles al agua. De igual forma, en la página 1238 se enseña que los ésteres de citrato causan irritación respiratoria, afectan el sistema nervioso, la presión arterial y el metabolismo del calcio. Por lo tanto, sin otra enseñanza el experto medio en la impresión offset al momento de la presentación de la solicitud no tendría ningún motivo para incorporar un plastificante de ester de ácido cítrico en un barniz o tinta de impresión offset, y mucho menos un **ester de un ácido policarboxílico**.

Teniendo en cuenta lo dicho anteriormente, solicito a usted lo siguiente:

- a) Que de conformidad con lo previsto por los artículos 3 (inciso 3); 35 (inciso 2) y 59 (inciso 2) del Código Contencioso Administrativo se consideren y se resuelvan TODOS los argumentos y TODAS las cuestiones planteadas así como las que aparezcan con motivo de este recurso.
- b) Que se revoque la resolución No. 9742 del día 28 de febrero de 2012 expedida por el Superintendente de Industria y Comercio, y se proceda a conceder el privilegio de patente de invención a la solicitud de mi mandante

Señor Superintendente,


DILIA RODRIGUEZ D'ALEMAN

CC. 41.654.882 de Bogotá

TP 20824

Cód. 008

IA
del Oficio de Registro

PRESENTACION PERSONAL

El anterior escrito fue presentado ante el
NOTARIO ONCE DEL CIRCULO DE BOGOTA D.C.

personalmente por *Diego Rodriguez*
Diego Rodriguez

quien exhibió la *41654882* *Bl*
y Tarjeta Profesional No. *20824* C.S.J. **10 ABR 2012**

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[Signature]

Guillermo Chávez Cristancho
NOTARIO



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The plasticizer market: an assessment of traditional plasticizers and research trends to meet new challenges

Mustafizur Rahman, Christopher S. Brazel*

Department of Chemical and Biological Engineering, The University of Alabama, Box 870203, Tuscaloosa, AL 35487-0203, USA

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Abstract

Plasticizers have long been known for their effectiveness in producing flexible plastics for applications ranging from the automotive industry to medical and consumer products. The plasticizer industry has grown with the use of plastics worldwide. Recent plasticizer research has focused on technological challenges including leaching, migration, evaporation and degradation of plasticizers, each of which eventually lead to deterioration of thermomechanical properties in plastics. Human exposure to certain plasticizers has been debated recently because di(2-ethylhexyl) phthalate, used in medical plastics, has been found at detectable levels in the blood supply and potential health risks may arise from its chronic exposure. The current paper presents a brief history and an overview of the traditional plasticizers currently available in the world market, discusses some of the problems associated with the end uses of these plasticizers and reviews recent scientific approaches to resolve these problems. The definition of an ideal plasticizer changes with each application; thus, this paper addresses technical issues first from a broad perspective, and then with a focus on leaching, migration, evaporation and degradation issues. Several approaches to reduce leaching and migration of plasticizers are discussed, including surface modification of plasticized polymers and the application of alternative plasticizers and oligomers to meet technological requirements. New approaches to reduce evaporation and degradation of plasticizers are discussed, with the aim of formulating long-lasting flexible plastics and minimizing the ultimate environmental impact of these chemicals. The development of fire-retardant plasticizers and novel plasticizers for use in biodegradable plastics are also included.

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Keywords: Plasticizer; Leaching; Migration; Degradation; Health risk; Surface modification; Alternative plasticizers; Fire-retardant plasticizers

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* Corresponding author. Tel.: +1 205 348 9738; fax: +1 205 348 7558.

E-mail address: cbrazel@coe.eng.ua.edu (C.S. Brazel).

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1. Introduction

In the past century, engineering plastics have progressed from novel invention to a major component in numerous industries. In recent years, engineering plastics have penetrated markets once dominated by metals and continue to grow in popularity with an average annual consumption growth rate of 5.09% [1]. The continuous use and growth of plastics depend on finding materials with unique and dependable properties that can be used efficiently and produced economically. Because of

the nearly limitless polymer structures and formulations that can be designed, the field of plastics is continually marked with technical innovations.

Both technically and economically, additives form a large and increasingly significant part of the polymer industry. Plasticizers account for about one third of the global plastic additives market in terms of consumption [2]. Used to increase structural flexibility, plasticizers have recently been scrutinized for environmental and health related problems. The expansion of plasticizing compounds to meet new material challenges, has also led to significant

technical advances. This paper highlights plasticizer research and development over the past 20 years.

2. Background

2.1. Attributes of plasticizers

The primary role of plasticizers is to improve the flexibility and processability of polymers by lowering the second order transition temperature [3]. Plasticizers are actually low molecular weight (MW) resins or liquids, which form secondary bonds to polymer chains and spread them apart. Thus, plasticizers reduce polymer-polymer chain secondary bonding and provide more mobility for the macromolecules, resulting in a softer, more easily deformable mass.

Plasticizers are incorporated in the amorphous parts of polymers while the structure and size of any crystalline part remains unaffected [4]. Plasticizers are expected to reduce the modulus, tensile strength, hardness, density, melt viscosity, glass transition temperature, electrostatic chargeability and volume resistivity of a polymer, while at the same time increasing its flexibility, elongation at break, toughness, dielectric constant and power factor [5]. Ideal plasticizers should be highly compatible with polymers, stable in both high and low temperature environments, sufficiently lubricating over a wide temperature range, insensitive to solar ultraviolet (UV) radiation, leaching and migration resistant, inexpensive and should fulfill health and safety regulations. The current market offers numerous choices of plasticizers with a range of attributes that can be selected for specific applications to meet critical material requirements.

Plasticizers can be either internal or external, where external plasticizer molecules are not attached to polymer chains by primary bonds and can therefore be lost by evaporation, migration or extraction. On the other hand, internal plasticizers are inherently part of the plastic and remain part of the product [6]. For both types of plasticizers, there is often a marked temperature dependence of material properties, though this is more pronounced with internal plasticizers. Internal plasticizers also have problems with retaining dimensional stability at elevated temperatures.

Plasticizers may also be divided into primary and secondary types [7]. Primary plasticizers are used as the sole plasticizer or as the major component of plasticizer, while secondary plasticizers are typically blended with primary ones to improve certain performance properties and/or to lower cost.

2.2. Evolution of plasticizers

The first man-made plastic known was manufactured in 1862 by Alexander Parkes in London, but it was not until the late 19th century when the concept of plasticizers was first introduced [8]. In the early days, manufacturers of celluloid or celluloid lacquers used natural camphor and castor oil for plasticization purposes, but those were unsatisfactory for many end uses. The discovery of triphenyl phosphate in 1912, later used as substitute for camphor oil, was a significant turning point that ushered in the era of ester plasticizers. The most important product that resulted from this early discovery was tricresyl phosphate which is still in use today. For some time, tributyl phosphate was highly regarded for cellulose derivatives, but it was eventually replaced by less volatile products. At the same time, glycerin acetates were developed but suffered the same fate due to their volatility. Phthalic acid esters found applications as plasticizers for the first time in 1920 and continue to be the largest class of plasticizers in the 21st century. Dibutyl phthalate (DBP) gained a dominant position amongst plasticizers which it held for many years and continues to hold today for polyvinyl acetate dispersions. Di(2-ethylhexyl) phthalate, DEHP, was introduced in 1930 and has been the most widely used plasticizer since the 1930s.

The driving forces for development of specialty plasticizers come from the extensive use of plastics in a wide range of applications, increased quality requirements, the need for materials that meet increasing rigorous product specifications and compatibility problems relating to particular products. Food legislation, health and industrial safety and commercial aspects play an important role and, over last 50 years, have led to the development of the vast range of plasticizers currently available. Initially a few fatty acid esters, benzoates, tartrates and chlorinated hydrocarbons were available to meet the new safety requirements. They were soon joined by esters

of adipic, azelaic and sebacic acid. These latter three immediately attracted interest because they considerably improved the cold fracture temperature of plasticized poly(vinyl chloride), PVC, the third most consumed polymer worldwide [9]. A large number of high performance plasticizers are produced now by systematic esterification of aliphatic or aromatic carboxylic acids.

2.3. Trends in plasticizer production

As the plastic industry continues to grow, so does the plasticizer industry. In the early 1990s, the annual US production of plasticizers averaged 2 billion pounds, of which 1.25 billion pounds were phthalates [10]. By 1999, the global demand for plasticizers had increased to 10.1 billion pounds, worth about US \$7 billion, while the total plasticizer demand in North America was 2.2 billion pounds [2]. Europe, North America, and Japan are currently the major consumers of plasticizers, and account for 28, 22, and 10% of the global demand, respectively. The current overall growth rate for production of plasticizers, as estimated in early 2000s, is about 2.8% per annum [2].

2.4. Current industrial plasticizers

The most frequently plasticized polymers include PVC, poly(vinyl butyral) or PVB, poly(vinyl acetate) or PVA, acrylics, cellulose molding compounds, nylon, polyamides and certain copolyamides. On average, PVC accounts for about 80% of all plasticizers consumed [11] (88% in Europe and 85% in North America [2]). The degree of plasticization of polymers is largely dependent on the plasticizer's chemical structure, including chemical composition, MW, and functional groups. Plasticizers that have low MW and a small number of polar groups generally provide higher flexibility and plasticization [12]. Plasticizers are generally chosen on the basis of the following criteria [8]:

- compatibility of a plasticizer with a given polymer,
- processing characteristics,
- desired thermal, electrical and mechanical properties of the end product,
- resistance to water, chemicals, solar radiation, weathering, dirt, microorganisms,

- effect of plasticizer on rheological properties of polymer,
- toxicity, and
- volume-cost analysis.

The most commonly used plasticizers worldwide are esters of phthalic acid (e.g. DEHP, diisodecyl phthalate or DIDP, diisotridecyl phthalate or DITDP, and diisononyl phthalate or DINP). With more than 30 different phthalates on the market, DEHP is by far the most widely used one. Phthalate esters have been used extensively in thermoplastic cellulose ester molding compounds, PVC and other vinyl chloride copolymers for over 60 years. Phthalates account for 92% of plasticizers produced worldwide while DEHP represents 51% of the phthalates [1]. In general, phthalates combine most of the desirable properties of a plasticizer such as [8]:

- minimal interaction with resins at room temperature,
- good fusion properties,
- satisfactory insulation for cables,
- produce highly elastic compounds with reasonable cold strength,
- relatively nonvolatile at ambient conditions, and
- low cost.

With phthalates, the polarizable benzene nucleus is highly effective with respect to compatibility with PVC, affording great flexibility to the polymer chains. However, compatibility decreases with the increasing length of the disubstituted alkyl esters. Shorter chain phthalates are easier to formulate because they diffuse faster, but have the drawback that they are more volatile [8]. The plasticizing effectiveness is reduced by branching and this effect is stronger the nearer the branches are to the polar group and the shorter the main chain becomes due to branching. This is paralleled by an increase in viscosity so that viscosity and plasticizer effectiveness are closely related. Terephthalates, oligoesters of *o*-phthalic acids and solid phthalate esters (e.g. dicyclohexyl phthalate and diphenyl phthalate) have some plasticizing properties, but are seldom used because of their high cost.

Phthalate esters were initially found to be benign to human beings [13] and therefore have been used in various products such as children's toys and medical

plastics where they may come in close contact with the human body. However, more recent reports have criticized these petroleum-derived products because of their suspected endocrine-disruption activity in laboratory rats, especially after phthalate plasticizers have been found to leach out of medical plastics such as intravenous (IV) bags and dialysis tubing [14]. A further discussion of medical issues is included later in this paper.

Phosphates are among the earliest known PVC plasticizers. They are also important for their additional flame retardant properties. They are less flammable than the phthalates probably because they form polyphosphoric acids by condensation reactions on heating and these cause charring reactions to occur in the polymer formulation [15]. Depending on their basic molecular structure, commercial phosphate esters can be grouped into three main categories: trialkyl, triaryl and alkyl/aryl phosphates. The triaryl phosphates improve the flammability properties of polymer formulations in which they are present but at the expense of increased smoke production. The alkyl and aryl phosphates also improve the flammability properties but unlike the triaryl derivatives, they do not increase smoke production when burnt in the air.

Other than phthalates and phosphates, there are several classes of plasticizers commercially available in the market, which offer different end properties to polymeric materials. Aliphatic dicarboxylic acid esters (adipates, azelates, sebacates) have high plasticizing effectiveness with PVC and PVA, and provide excellent low temperature flexibility. However, they are only effective in a narrow MW range. These types of esters with MW of 300–350 tend to be too volatile for many applications, while those with MW over 400 tend to be incompatible with polymers [16]. Monocarboxylic acid esters of polyols show good plasticizing properties too. Epoxidized fatty acid esters have been used as plasticizers and also as stabilizers for PVC due to their ability to form bonds with the hydrogen chloride that results from the decomposition of PVC. Trimellitates, paraffinic sulfonic acid and phenyl esters, polyesters, chlorinated hydrocarbons, aliphatic/aromatic monocarboxylic acid esters such as benzoates, and a variety of elastomers have also been used as plasticizers for years.

Plasticizers continue to evolve with the demand of specialty applications. This evolution has recently been spurred by the controversy over the safety of many traditional plasticizers [14]. This has led to the emergence of novel plasticizers including citric acid esters, oligomers and polymeric plasticizers, epoxidized soybean oil, PVC/EVA (ethylene vinyl acetate) graft polymers and terpolymers, many of which have become commercially available over the past two decades. Thus, a plethora of plasticizers is available to choose from, depending on the processability and end-use requirements. Table 1 summarizes the major categories of plasticizers giving specific examples and some common end uses for the plasticized materials, while Fig. 1 shows the structures of some commercially available plasticizers.

3. Technical challenges for the plasticizer industry

As the plasticizer industry has matured, a number of technical challenges have been addressed to improve formulations, solve technical end-use problems or meet new requirements. Some of the problems include evaporation or degradation of traditional plasticizers due to their volatility or UV susceptibility, leaching of plasticizers to polar and nonpolar liquid media, migration of plasticizers to other polymeric substances and surroundings, insufficient lubrication at subzero temperatures and suspected carcinogenic effects on a number of living organisms. Table 2 summarizes some of the current technical challenges for the plasticizer industry. The fundamental bases for these problems are chemical in nature; many are related to molecular thermodynamics, transport properties and interfacial phenomena. Current plasticizer research focuses on these technical issues from different perspectives.

3.1. Aspects of leaching and migration of plasticizers

Leaching and migration of plasticizer molecules from polymers is a critical issue that determines a material's usable lifetime. Leaching, by definition, refers to the removal of a substance from a solid via a liquid extraction media. Migration, on the other hand, refers to any method by which a component leaves a material—to a gas, liquid or solid phase. In this paper,

Table 1
Properties and applications of some commercial plasticizers [1,6,8,10,16–19]

Plasticizer type	Main characteristics	Common examples	End uses
Phthalates	Excellent compatibility, high gelling capacity, low volatility, water resistant, inexpensive *terephthalates have high migration resistance	DEHP, DIDP, DINP, DITDP, DBP	Medical plastics (IV bags and tubing), kitchen floors, vinyl wall coverings, carpet backing, wires and cables, toys, hoses, shower curtains, food packaging, automobile parts
Phosphates	Flame retardant, heat resistant, highly solvating for vinyl resin, lower fusion temp. than DEHP, but accelerates thermal degradation of PVC, not suitable for low temp. and food-contact applications	Triphenyl phosphate, tris (2-ethylhexyl) phosphate, tricresyl phosphate, Kronitex®	Flame retardant plasticizer in calendered goods, extrusions, plastisol-derived products with nylon, sulfonamides and other highly polar compounds, PVC, polyacrylates, cellulose derivatives, synthetic rubbers
Adipates	Low viscosity, higher gelation and fusion temp. than DEHP, cause less brittleness than phthalates, relatively volatile and extractable, but give superior low temp. flexibility	Dibutyl adipate, bis(2-ethylhexyl) adipate or DEHA, diisodecyl adipate	In combination with phthalates, improved low temp. (even arctic) flexibility for automobile parts and aircraft interiors
Azelates	Improve low temp. flexibility, less water sensitive than adipates	Bis(2-ethylhexyl) azelate	With cellulosic resins and elastomers, food-contact applications with PET and polyester
Sebacates	Excellent low temp. performance	Dibutyl sebacate, dioctyl sebacate	Dibutyl sebacate used specially for polyisoprene; food contact, medical, and pharmaceutical plastics
Epoxidized fatty acid esters	Impart cold strength, very low volatility, pigment dispersing agents in plasticized PVC, synergistic thermostabilizing effect with Ca–Zn stabilizers, can stabilize other plasticizers by offering migration resistance	Butyl epoxystearate, cyclohexyl epoxystearate	Low temp. applications of PVC and its copolymers
Benzoates	Highly solvating, low moisture sensitivity, excellent resistance to organic extraction, excellent stain and UV resistance, good gelation properties, desirable environmental, health and safety profiles, high viscosity (limits application)	Benzoplast®, Benzoflex®	Vinyl flooring, PVA adhesives, PU castable and sealants, latex caulks, coatings, plastisol formation, processing aids, inks, hot melt adhesives
Polyesters/polymeric plasticizers (MW between 850–3500)	Very low volatility, highly resistant to extraction and migration, extend lifetime of flexible articles, improve weathering resistance, highly viscous and usually blended with lower viscosity plasticizers	Poly(1,3 butyleneglycol adipate), poly(ethylene glycol) PEG, Admex®, Paraplex®	Compatible with PVC, cellulose acetate butyrate and cellulose nitrate, used in vinyl dispersions, films, sheet, floor coverings, cable insulation and sheathing resins only where oil and fat resistance is required
Trimellitates	Low volatility, good water resistance, high temp. stability, similar to phthalates in compatibility and plasticizing effectiveness, less migration tendency, extraction by oils and hydrocarbons as high as phthalates, high price	Trioctyl trimellitate (TOTM), octyl dibenzyl trimellitate	PVC tubes, blood storage bags, haemodialysis tubing, catheters
Sulfonic acid esters and sulfamides	Less volatile than phthalates, tend to discolor, weather resistant, sulfonic acid esters have slightly better gelation effectiveness than DEHP, good hydrolytic resistance in alkaline solution, arylsulfonamides not compatible with PVC	<i>n</i> -Butyl benzenesulfonamide, toluenesulfamide	Sulfonic acid esters used with PVC, sulfonamides used specially with polyamide and cellulose based molding resins

(continued on next page)

2

Table 1 (continued)

Plasticizer type	Main characteristics	Common examples	End uses
Monocarboxylic acid esters	Esters with low alkanols are too volatile, sensitive to water, and show poor gelation properties, longer chain esters of fatty acids are not too compatible with polymers	<i>n</i> -Butyl formate, ethyl lactate	Important as low temp. secondary plasticizers and as lubricants in processing rigid and plasticized PVC
Epoxidized vegetable oils	Heat and light stability, resistant to extraction, epoxidized soy bean oil has high MW (~1000) and bulky structures which resist migration	Epoxidized soy bean oil (ESO), epoxidized linseed oil, tallates	Primarily as heat stabilizers
Chlorinated hydrocarbons	Somewhat flame retardant, limited compatibility, often colored, have odor; aromatic—high viscosity, fairly good compatibility, poor heat and light stability; aliphatic—low viscosity, may exude from aged fused products	Polychlorinated biphenyls (PCBs), polychlorinated 1-dodecene, 1-tetradecene, 1-hexadecene	Mainly used as secondary plasticizers; for cost reduction in blends and to achieve some flame retardancy
Citrates	Good solvating power for PVC and cellulose acetate, high efficiency, non-toxic, non-acetyl citrates are relatively volatile and water sensitive compared to DEHP, good for medical plastics if not exposed to high lipid media	(acetyltri- <i>n</i> -hexyl citrate) Citroflex® A-6, (<i>n</i> -butyryltri- <i>n</i> -hexyl citrate) Citroflex® B-6	With cellulose, PVC, PVA, and other polymer films and flexible tubings used in medical plastics and food-contact plastics
Oligomers (low MW polymers)	Offer better extraction and migration resistance, lower volatility, weathering resistance and reduced odor, may exude particularly at high temp. and humidity	(recorcinol bisdiphenyl phosphate) Fyrolflex® RDP-B, poly (butadiene dimethacrylate)	Automotive, marine and aeronautical applications
Polymerizable plasticizers	Polymerize at elevated temp. during the gelling of PVC	Allyl phthalate, acrylic esters, monochlorostyrene	Toys, shoe heels and certain industrial articles that must have high stiffness
Elastomers	Used instead of or together with low MW plasticizers for PVC to improve resistance to migration, saponification, low temp. flexibility, mechanical and oxidative stability at high temperatures	Nitrile rubber, ethylene/vinyl acetate copolymers, acrylonitrile/butadiene/styrene terpolymers	Coverings of instrument panels, cushion covers, shoe soles, insulations for cables, tubes and articles for aircraft interior

leaching will be used to refer to any liquid extraction of a plasticizer while migration will refer to any gas or solid-phase transfer of plasticizer.

Plasticized polymers are often in contact with stationary or flowing fluids, or in contact with some other solid material. In the course of time, plasticizers tend to diffuse down the concentration gradient to the interface between the polymer surface and the external medium. In many instances, the interfacial mass transport to the surrounding medium has been found to be the limiting step rather than diffusion of plasticizer through the matrix to the surface. This rate is usually a function of temperature and initial plasticizer concentration while the rate of migration (permeation) is a product of solubility and diffusion coefficients [20]. Whether the plasticizers leach out to a liquid, or migrate to gaseous or solid substance,

polymers fail to retain their flexibility while the loss of plasticizers leaves the polymers inappropriate for the desired application. In addition, the plasticizers coming out of the polymers often pose health and environmental risks, as described in a later section. Leaching and migration issues are indeed one of the toughest challenges regarding research in the plasticizer industry today.

3.2. High temperature flexibility

Most flexible plastics are limited in their end use because plasticizers are generally low-to-medium MW chemicals with measurable vapor pressure below their boiling points. This often causes the plasticized materials used in high temperature environments to be replaced frequently, as they become brittle and tend

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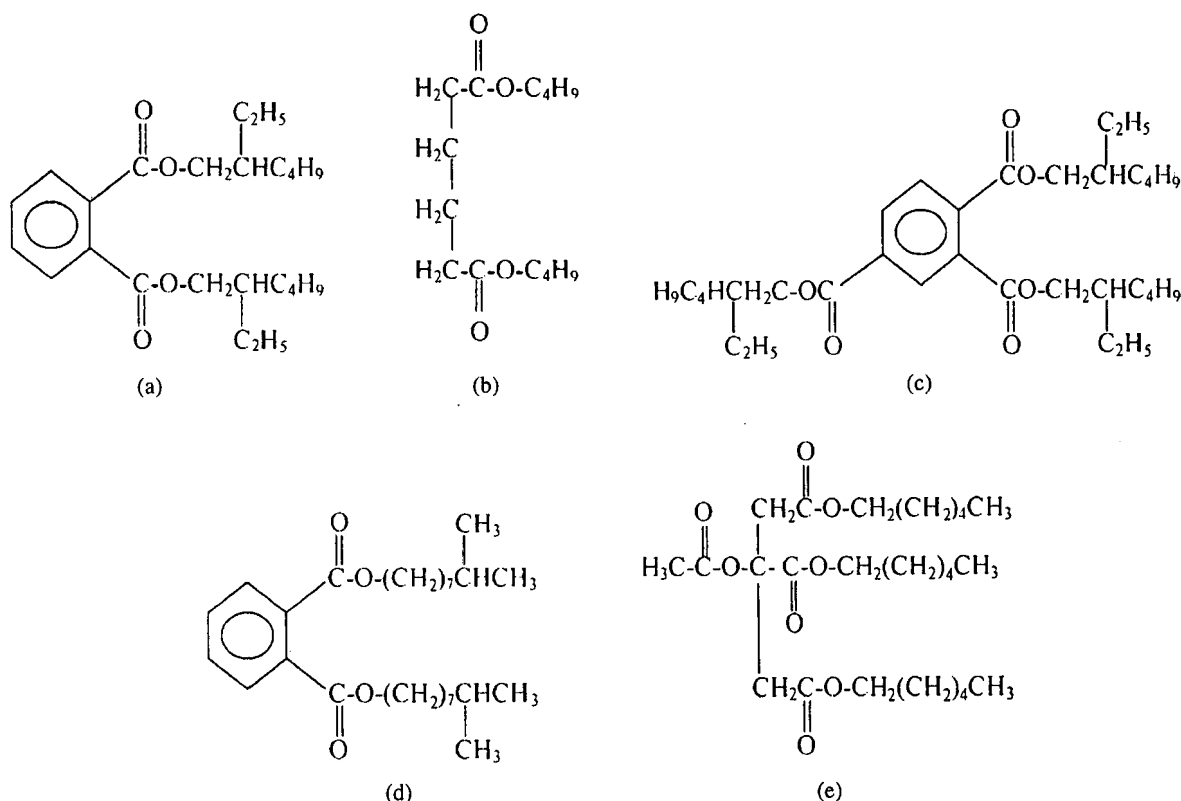


Fig. 1. Structures of some traditional plasticizers: (a) di(2-ethylhexyl) phthalate, (b) dibutyl adipate, (c) trioctyl trimellitate, and (d) acetyltri-n-hexyl citrate.

to crack owing to evaporation or degradation of plasticizers. In addition to degradation of plasticizers, some polymers, e.g. PVC, are also susceptible to high temperature environments. The thermal degradation and dehydrochlorination of PVC have been widely studied since the 1940s [21]. Thermal dehydrochlorination of PVC begins with internal allylic chloride

and tertiary chloride structural defects formed during polymerization [22]. The initial stage of thermal degradation of PVC involves sequential loss of hydrogen chloride accompanied by the generation of conjugated polyene sequences and followed by a series of polyene growth steps through an ion-pair or quasi-ionic route. Phthalate esters, in addition to plasticization, have been found to reduce the rate of dehydrochlorination of PVC by inhibiting the growth of polyene sequences. Hence, when they evaporate from the PVC host, discoloration, tackiness and embrittlement result. The development of new plasticizers that are not subject to thermal aging will allow the use of flexible polymers at temperatures higher than what is currently possible.

3.3. Low temperature lubricity

The low temperature performance of plasticizers can cause problems with sealing plastics such as

Table 2

Plasticizer-related technical challenges

1. Migration out of plastic
 - a. Solid-solid migration
 - b. Evaporation
 - c. Liquid leaching
2. High temperature flexibility
3. Low temperature lubricity
4. Health and environmental effects (cytotoxicity)
5. Flammability concern regarding plasticizers
6. Compatibility with new polymers
7. Stability to ultraviolet rays
8. Biodegradability
9. Improved material lifetime

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gaskets, which may become brittle and crack in cold environments. Plasticizers work effectively to lower the glass transition temperature of the host polymer, but the degree to which the T_g is reduced depends on the thermodynamic compatibility of the plasticizer with the polymer (the greater this compatibility, the more plasticizer can be added to the formulation, which increases lubricity). An additional problem at low temperatures is that many plasticizers have melting points close to room temperature, and they may freeze (solidify) before the polymer passes through a T_g . Therefore, low temperature lubricating plasticizers can provide polymeric materials with new and improved applications.

3.4. Health and environmental effects of plasticizers

Human and environmental exposure to plasticizers can occur in different ways. The most prevalent causes of these exposures include point-source pollution from plasticizer manufacturing or plastic formulation, and leaching, migration and evaporation of plasticizers.

Phthalate plasticizers have been a target of worldwide scrutiny in the past two decades from consumer and environmental groups on the grounds of potential carcinogenicity and possible endocrine modulating effects [14]. PVC-based medical plastics have received the most attention partly because medical uses constitute 10% of the phthalate plasticizer market [23]. The PVC used in IV and blood storage bags typically contain 30–40 wt% DEHP and medical tubing such as dialysis tubing may contain as much as 80 wt% DEHP [24]. This DEHP has been shown to leach out of PVC depending on temperature, amount of plasticizer present, agitation of the device, storage time while in contact with medical solutions, and the type of medium being stored in or moving through the medical device.

DEHP leaching from medical plastics was first observed in late 1960s when Jaeger and Rubin found that one pint of blood and its anticoagulant solution may contain 6 mg of DEHP after being stored in PVC blood bags for 21 days at 4 °C [25]. Another study by the same authors in 1972 showed that DEHP was extracted from PVC blood bags by human blood at a rate of 2.5 mg/l per day at the typical blood bank storage temperature of 4 °C [26]. Extensive research began after the International Agency for Research on

Cancer classified it as ‘possible carcinogenic to humans’ in 1980 based on early studies on rodents [1]. Subsequently, numerous experiments were conducted to examine the testicular and ovarian toxicity, as well as the embryotoxicity, nephrotoxicity, cardiotoxicity, pulmonary toxicity, and hepatotoxicity of DEHP in mammals [24]. Results proved it to be a possible carcinogenic substance, but it has been found that the maximum safety limits required for consumer products are at least 75 times lower than a hazardous concentration.

Leaching of DEHP from plasticized PVC has been observed in soapy water, cottonseed oil, and also in high humidity environments [24]. While losses in aqueous solutions are small, these percentages are not insignificant especially considering the lifetime exposure and bioaccumulation of DEHP. Particular concern has been raised in neonatal care applications because newborns receive among the highest doses of DEHP from blood transfusions, extracorporeal membrane oxygenation and respiratory therapy [27,28]. Using the typical PVC-DEHP tubing and EVA bags with PVC-DEHP connections, it has been found that infants and children receiving intravenous total parenteral nutrition (TPN) infused through PVC-administration sets potentially receive considerable amounts of DEHP every day. DEHP is extracted from the bags and tubing due to the high solubility of DEHP in lipids and DEHP extraction by TPN depends on the lipid content of each TPN preparation and the flow rate [29]. Table 3 shows the amount of DEHP received by a 2 kg baby in 24 h with different amounts of TPN solutions, using typical DEHP-plasticized PVC infusion lines [28].

Adults can also be subjected to DEHP exposure from medical plastics. Kambia et al. [30] studied the leachability of DEHP from PVC haemodialysis tubing during maintenance haemodialysis of 10 patients with

Table 3
Daily doses of DEHP received by a 2 kg baby during TPN infusions

Solution	Amount (ml)	DEHP load (μg)
Aminoacid/glucose	140	116.2
Lipid emulsion, 20%	24	10,185.6
Midazolam	24	26.4
Fentanyl	28.8	132.5
Propofol 1%	10	6561.0

chronic renal failure. The patient blood obtained from the inlet and the outlet of the dialyzer was analyzed during a 4 h dialysis session. An average DEHP quantity of 123 mg was extracted from tubing during a single dialysis session, of which approximately 27 mg was retained in the patient's body.

Phthalates are also used in baby-care products and toys which represent around 1% of the phthalate plasticizer market [23]. Since young children put the plastic-toys in their mouth, the plasticizers can leach out and be swallowed, which has led to the investigation of low toxicity plasticizers. Fortunately, DEHP exposure in this way is considerably less than the critical limit of 69 mg/kg per day [1].

Human exposure to DEHP also occurs through inhalation of air due to off-gassing from PVC products such as flooring and car dashboards, drinking water contaminated with DEHP, and through the ingestion of food containing DEHP that has leached out of packaging. Contact between food and plastic packaging may often cause reciprocal transfer between the material and the surrounding medium. In the case of PVC-based commercial wrap films or containers, various processing aids like plasticizers may exude from the packaging material or can be extracted by the foodstuff [31]. Apart from the alteration in chemical and physical properties of the plastic material, this phenomenon causes contamination of the packaged food which eventually ends up inside human body.

Oral LD₅₀ values for DEHP have been reported as 25 g/kg in rats and 30 g/kg in mice [24]. As mentioned earlier, a detrimental dose for humans has been estimated at 69 mg/kg per day whereas the average daily exposure to DEHP is much lower (2.3–2.8 µg/kg in Europe and 4 µg/kg in the US) [1]. Because this figure does not include workplace air exposures or indoor air exposures from off-gassing of building materials, there is a possibility that some people could be at a greater risk, especially with an estimated 500,000 pounds of DEHP released to the environment from US manufacturing facilities in 1997 alone [24]. Also, daily exposure to DEHP in medical settings may exceed general population exposures by up to three orders of magnitude [14].

In addition to toxicity-related problems, application of DEHP as plasticizer was found to have adverse effects on the biocompatibility of the plastic materials used in medical devices. Upon contact with

blood, albumin is instantly absorbed on the polymer surface, followed by globulin [32]. Pengerovski et al. [33] have established that the surface of a polymer material that has already absorbed a layer of albumin attracts thrombocytes to a greater extent. Elsewhere, it was found from both in vitro and in vivo studies that in plasticized PVC, an increase in DEHP content leads to deterioration in the material's biocompatibility [34]. In addition to the increased protein deposition found on PVC surfaces with increasing DEHP content, blood coagulation time and hemoglobin concentration in blood were found to decrease during storage of blood in DEHP plasticized PVC bags. This is probably due to the higher concentration of DEHP that migrated onto the surface of the samples.

Beyond the concerns over the use of phthalates in the medical field and other household applications, these plasticizers have also been noted to have an adverse environmental impact on plants as cellulose acetate filters plasticized with diethyl phthalate (DEP) showed severe phytotoxicity in Ashley cucumbers when exposed to UV-B rays ($\lambda=290\text{--}320\text{ nm}$) [35]. Hence, preventing leaching and migration of plasticizers will have considerable impact on the environment as well as human health.

3.4.1. Government regulation of phthalates

The regulation of phthalates as plasticizers has undergone scrutiny with the concerns over the toxicity and carcinogenic behavior of DEHP. Because these compounds have been used safely for an extended period, there are some disagreements among the different regulating agencies over the urgency to find suitable replacements to DEHP as plasticizers. The European Union Scientific Committee of Toxicity, Ecotoxicity and the Environment announced in 1998 that there were safe migration limits for phthalates [1]. In a scientific opinion, the committee stated that the phthalate plasticizers can safely be used in production of soft PVC-based toys, provided that migration limits are observed. Parallel to the European conclusions, the American Council on Science and Health convened a scientific panel of health experts, which concluded that the phthalate plasticizers used in PVC medical devices are neither carcinogenic nor have any harmful effect at the levels to which consumers are exposed [1]. Also, a scientific panel convened by the US Consumer Product Safety Commission concluded

that DINP, the most used plasticizer in PVC-based toys, does not pose a health risk to children at the typical level of exposure [36]. However, the concern over DEHP has led the US Food and Drug Administration (FDA) to suggest that manufacturers either label certain devices with their DEHP content or consider the feasibility of replacing PVC containing DEHP with alternative materials or different plasticizers, or using coatings that may minimize patient exposure to DEHP [37]

3.5. Flammability concern regarding plasticizers

Traditionally-used plasticizers are generally hydrocarbons and often make the polymers more susceptible to fire hazards. The aliphatic components of plasticizer molecules, especially if they are linear, have better plasticizing properties than aromatic compounds but they are, in general, more flammable [15]. Because of the flame-retardant properties of chlorine atoms, PVC usually requires much less flame-retardant additives than do other polymers. However, since PVC is frequently used in plasticized forms, the flammability of the plasticizers is a major concern. Phthalate plasticizers such as DEHP, when compounded into PVC formulations, increase smoke production, ease of ignition and the burning rate. Application of less or nonflammable plasticizers is therefore one of the main foci of current plasticizer research.

3.6. Compatibility with new polymers

As novel polymers are developed and new applications require the plasticization of polymers that have not been used in flexible plastics, plasticizers must evolve to be compatible for a range of new formulations. As has already been discussed, the plasticizing efficiency and thermodynamic compatibility of plasticizers with polymers depend on a number of properties such as chemical structure, MW, functional groups, alkyl chain length and diffusion and solubility parameters of the plasticizers. Therefore, plasticizers must have sufficient thermodynamic compatibility with the host polymers in addition to providing desired flexibility and other end-use properties to the polymeric materials.

3.7. Stability when exposed to ultraviolet rays

Apart from leaching, migration and thermal aging, degradation of polymeric materials by UV rays may also cause a reduction in plasticizing efficiency. Plastics are often subjected to harsh environments that can cause evaporation of plasticizers, as often observed in automotive dashboards. Many dashboards lose plasticizers and crack over years of exposure to UV rays from sunlight and temperature cycles. Degradation of PVC is particularly important for this discussion as it has been found that plasticized PVC degrades more rapidly than unplasticized PVC in the near UV region ($\lambda > 290$ nm) [16].

3.8. Plasticizers for biodegradable polymers

Biodegradable polymers have gained much attention for environmental and biomedical applications. When disposed in biologically active environments, biodegradable polymers are completely converted to biological products (biogas, humic matter, biomass, etc.) within a certain period of time. These polymers, as well as their degradation products, must cause no deleterious effects on the environment. Fully biodegradable synthetic polymers such as poly(lactic acid) or PLA, polycaprolactone, and polyhydroxybutyrate-valerate have been commercially available since 1990 [38]. Plasticizers are used for biodegradable plastics as well. There are more stringent requirements on these plasticizers, though, since by definition they will be released to the environment during normal product use. Health and safety issues dominate the research in this field, with benign, often natural substances having nearly as great importance as the ability to lower the T_g of the polymer. Because of the prevalence and commercial applications of biodegradable polymers, recent research has focused on developing compatible plasticizers that also biodegrade.

3.9. Improved material lifetime

By preventing plasticizer loss and degradation, and by improving thermodynamic compatibility of plasticizers with polymers, the lifetime of flexible plastics can be increased. This results in reduced costs and fewer plastics that must be landfilled annually.

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4. Approaches to meet plasticizer challenges

Current research trends in the plasticizer industry represent approaches to solve the technical issues discussed in Section 3. Many of the issues are interrelated; thus, novel plasticizers and material modification often seek to solve multiple shortcomings. While the plasticizer industry grows, these technical challenges are dealt with from different perspectives in terms of the diversified applications of plastic materials.

4.1. Approaches to reduce plasticizer leaching and migration

Several approaches have been developed to reduce the leaching of plasticizers into physiological fluids as well as different organic and inorganic solvents and also to reduce the migration of plasticizers into solid and gaseous media. These techniques vary in level of complexity and also cost. Some methods that have successfully reduced leaching are broken down in Table 4.

4.1.1. Surface modification

Surface modification of polymers has attracted great attention in biomaterial research because it can improve the biocompatibility of a polymer without compromising the mechanical properties. This technique has also been employed to reduce or prevent leaching and migration of plasticizers from polymers.

4.1.1.1. Surface crosslinking. Surface crosslinking is one of the most common techniques studied to prevent leaching and migration of plasticizers. The cross-linked polymer-surface actually acts as a barrier to

Table 4
Major methods investigated to reduce plasticizer leaching and migration

1. Surface modification
a. Surface crosslinking
b. Modification of surface hydrophilicity/lipophilicity
c. Surface coating
d. Surface extraction
2. Use of polymeric plasticizers and oligomers
3. Use of alternative plasticizers
4. Alternative polymers

interfacial mass transport of plasticizer molecules. Audic et al. [39] investigated the effect of plasma-induced surface crosslinking of PVC-based flexible films to limit plasticizer leaching from packaging into fatty foodstuffs. Leaching tendencies of DEHA and ESO from PVC films to isooctane were monitored by supercritical fluid chromatography. Simultaneously, the effect of replacing DEHA with an elastomeric terpolymer, poly(ethylene-*co*-vinyl acetate-*co*-carbon monoxide) or EVACO, Elvaloy 742®, was observed. It was found that the percentage leaching of plasticizers decreased with increasing plasma-treatment time. Best results were shown with Argon plasma (Fig. 2). Argon plasma-treated PVC films showed significant leaching resistance which can be attributed to the high degree of crosslinking during plasma treatment and further formation of oxygen-based functional groups when the samples were re-exposed to air. Partial replacement of DEHA by EVACO led to higher migration of DEHA, but it was reduced considerably after the plasma-treatment. Surface crosslinking of polymer to reduce leaching and migration is often employed along with other surface modification techniques, as will be shown later in this chapter.

4.1.1.2. Modification of surface hydrophilicity/lipophilicity.

The nature of polymer surface often governs

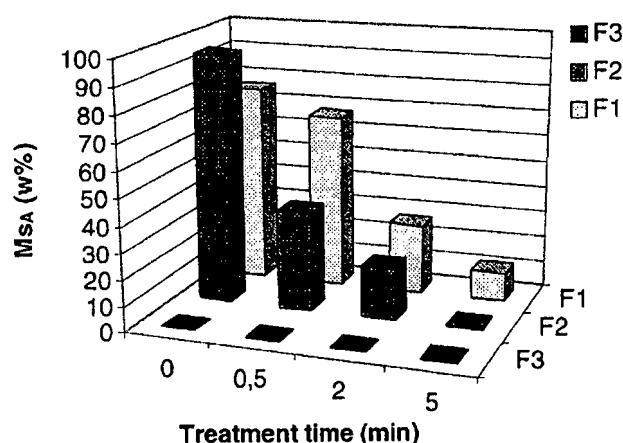


Fig. 2. Percentage-leaching of DEHA from PVC films to isooctane with increasing Argon plasma-treatment time. F1 films contain 28 phr DEHA and no EVACO, F2 films contain 10 phr DEHA and 40 phr EVACO, and F3 films contain no DEHA and 60 phr EVACO. Reprinted from Ref. [39], © (2001), with permission from John Wiley and Sons, Inc.

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the interaction of the polymer with certain liquid media. Leaching of plasticizers from polymer into a liquid can therefore be controlled by regulating surface characteristics. Among a variety of surface modification techniques, grafting of water soluble polymers to the surface of biomaterials has been attempted by a number of researchers. For example, Krishnan et al. [40] grafted *N*-vinyl pyrrolidone onto flexible PVC sheets used in medical applications using ionizing radiation from a ^{60}Co source. The leaching of the plasticizer DEHP into a strong organic extractant, *n*-hexane, was significantly reduced in different grafted PVC systems at 30 °C. Incorporation of ethylene dimethacrylate as a crosslinking agent during grafting further reduced the plasticizer leaching.

Leaching resistance of flexible PVC has also been improved by grafting PEG, which is often used in biomaterials to prevent biological recognition and protein adhesion [41]. Surface-modified plasticized PVC sheets and tubes were formed by the classical Williamson ether synthesis reaction where PVC was treated with an excess of Na-PEG. Leaching of DEHP from PVC to petroleum ether, cottonseed oil and paraffin oil was reduced considerably for PVC grafted with Na-PEGs with MW 400 and 4000. The decrease in plasticizer leaching after PEG-grafting is presumably due to the hydrophilic PEG surface acting as a barrier to the diffusion of DEHP from the PVC matrix. Fig. 3 shows the reduced leaching of DEHP into cottonseed oil and paraffin oil due to grafting of PVC with PEG 400 at 70 °C.

Another surface modification technique that has been found to be effective in preventing leaching of plasticizer is the nucleophilic substitution of chlorine in plasticized PVC by sodium azide in aqueous media and using tetrabutyl ammonium bromide as the phase transfer catalyst [42]. The azidated PVC surface was then irradiated using UV rays with a 125 W lamp for various time periods to crosslink the surface. Leaching of DEHP from the surface-modified PVC into hexane was reduced considerably depending on the extent of azidation of the PVC surface and the irradiation dose. However, there was pronounced change of color of the PVC samples due to substantial dehydrochlorination that occurred during the grafting process and 35% reduction in elongation at break resulting from the surface crosslinking of PVC.

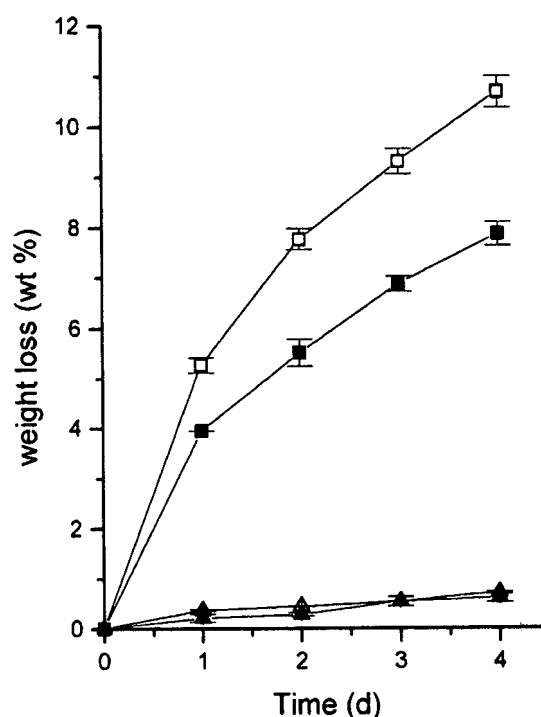


Fig. 3. Kinetics of leaching of DEHP from DEHP-plasticized PVC tubes to cottonseed oil and paraffin oil at 70 °C. [unmodified PVC tubes in cottonseed oil ($\square$), and in paraffin oil ($\blacksquare$), and PEG 400-grafted PVC tubes in cottonseed oil ($\triangle$), and in paraffin oil ($\blacktriangle$)]. Reprinted from Ref. [41], © (1998), with permission from Blackwell Publishing Ltd.

Nucleophilic substitution to surface-crosslink plasticized PVC was also studied by replacing chlorine atoms in medical grade PVC tubes with thiosulfate anions in aqueous media in the presence of a phase transfer catalyst, tetrabutylammonium hydrogen sulfate [43]. Tubes were then sterilized by autoclaving and by gamma irradiation. This treatment resulted in a hydrophilic polymer surface, which showed significant leaching resistance for DEHP in hexane (Table 5). This can be attributed to the presence of hydrophilic sulfonate and thiosulfate groups on the surface acting as a barrier to diffusion of the plasticizer as well as to some extent the surface crosslinking, caused by chain scission during gamma sterilization. However, the surface-modified PVC showed accelerated leaching of DEHP in cottonseed oil and PEG 400. This modified PVC surface was also found to be cytotoxic in nature and therefore cannot be used in contact with living tissue.

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Table 5

Amount of DEHP leached out into hexane at 30 °C from thiosulfate-substituted PVC tubes subjected to different modes of sterilization[40]

Sample	Mode of sterilization	Incubation time in hexane	DEHP migrated ^a (wt%)
Unmodified PVC	Unsterilized	24 h	27.07 ± 0.8
Unmodified PVC	Autoclaved	24 h	27.32 ± 0.9
Unmodified PVC	Gamma	24 h	25.88 ± 0.4
Thiosulphate substituted PVC	Unsterilized	30 days	0.14 ± 0.002
Thiosulphate substituted PVC	Autoclaved	30 days	0.18 ± 0.005
Thiosulphate substituted PVC	Gamma	30 days	0.02 ± 0.008

^a Average of three determinations.

4.1.1.3. Surface coating. Leaching and migration of plasticizers from polymer surface can be reduced by coating the polymer surface with some non-migrating material. But these coatings are usually thick and may often cause a reduction in flexibility of the polymeric materials. However, a surface modification technique that could be useful to prevent leaching and migration of plasticizers is chemical vapor deposition (CVD), which is generally used to coat complex substrates like fibers or the inner surfaces of tubes. Usually, CVD requires high coating temperatures, which make it impossible to coat temperature-sensitive materials like polymers with titanium (Ti)-based layers. But a new plasma-assisted chemical vapor deposition (PACVD) process was developed to coat polymers at very low temperatures with Ti-based layers [44]. PVC and five other commercial polymers were coated using the precursor $\text{Ti}[\text{N}(\text{C}_2\text{H}_5)_2]_4$ with the carrier gases hydrogen (H_2) and nitrogen (N_2). The coating was found to be an effective diffusion barrier to prevent leaching of DEHP from PVC. Additionally, the Ti–C–N coatings have the potential to improve the blood compatibility of polymers. Besides medical applications, this new coating makes it possible to improve the wettability, corrosion stability or electrical conductivity of polymers.

4.1.1.4. Surface extraction. The removal of plasticizer from the polymer surface by surface extraction is another method proven successful at reducing diffusion and leaching in polymer systems [45,46].

In surface extraction, a material is briefly exposed to a solvent for the plasticizer, and then dried. This leaves the polymer with a non-uniform distribution of plasticizer and a rigid surface which blocks interfacial mass transfer of the plasticizer. However, this rigid surface affects the flexibility of the polymer to some extent. Fugit et al. [47] proposed this technique to resist the leaching of plasticizer from plasticized PVC. Plasticized materials were first briefly soaked in *n*-heptane and then dried. Both the extraction and drying times and temperatures were varied to find the optimum result. This treatment reduced the leaching of DEHP from plasticized PVC into liquid food or a stimulant by more than 50%, and also introduced a significant lag time for leaching, as shown in Fig. 4. While this technique may be useful for sporadic exposure to a solvent, it is not a solution that prevents leaching permanently.

While different surface modification technique discussed in this section were found to successfully prevent leaching of plasticizers into different solvents, there are a number of trade-offs that can change other polymer properties such as flexibility, thermal stability, surface characteristics and appearance. These properties, along with the added expense of any of these treatments, must be considered so that optimal materials can be designed for each application.

4.1.2. Polymeric plasticizers and oligomers

Polymeric plasticizers have a great advantage in their inherent low volatility and are now being studied as replacements for traditional plasticizers. They can be designed so that they are highly compatible with the host polymer, and leaching and volatility issues have been significantly improved over traditional plasticizers. However, polymeric plasticizers are usually expensive and have lower plasticizing efficiency than most traditional plasticizers.

In a long-term study, medical grade PVC, plasticized with a 58 phr polycaprolactone-polycarbonate (PCL-PC) blend of $M_n \sim 32,700$, experienced negligible leaching while samples were kept in water or phosphate buffer at 37 °C for 98 days [48]. Only a trace amount of 6-hydroxyhexanoic acid, the final hydrolysis product of PCL-PC, was detected in the leachate and there was no notable weight loss. Even when the aging temperature was raised to 70 °C, only a minor increase in the amount of 6-hydroxyhexanoic

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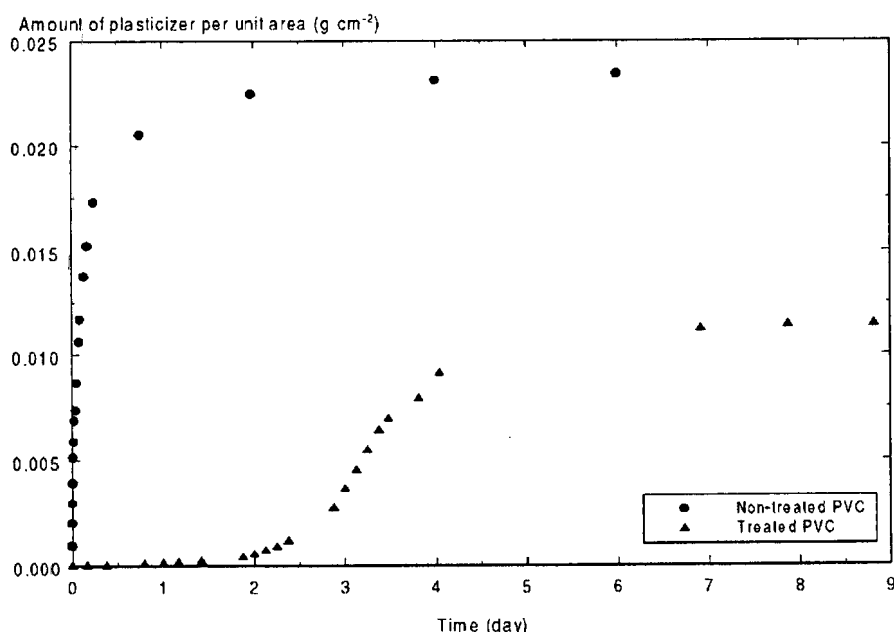


Fig. 4. Amount of DEHP (per unit surface area of PVC samples plasticized with 35 wt% DEHP) leached out into *n*-heptane from surface-extracted and non-extracted PVC sheets at 30 °C. Reprinted from Ref. [47], © (2003), with permission from John Wiley and Sons, Inc.

acid was observed and the weight loss after 98 days was less than 1%.

While the observation that polymeric plasticizers can reduce leaching is not surprising, the MW of polymers incorporated as plasticizers plays an important role in determining the properties of the end product. It has been found that the flexibility of the polymeric material as well as diffusion and migration of plasticizer within the host polymer is directly related to the MW of the polymeric plasticizer used. The polymeric plasticizer poly(1,3-butylene adipate), PBA, was found to have better migration resistance than DEHA and DEHP, plasticizers typically used in PVC-based cling films [49]. Shah et al. [50] also studied the effect of replacing DEHP by the polymeric plasticizer PBA ($M_n = 1200$), in PVC. It was found that PBA induced significant resistance to leaching in petrol and kerosene (Fig. 5) and migration resistance to silica (Fig. 6). PBA's extraction resistance was attributed to its higher MW. A study of the leaching of different MW PBA plasticizers from a PVC film into olive oil indicated preferential leaching of the lower MW species [51]. The oligomers with MW between 300 and 1100, which comprised 24% of the parent plasticizer, accounted for more than 90% of

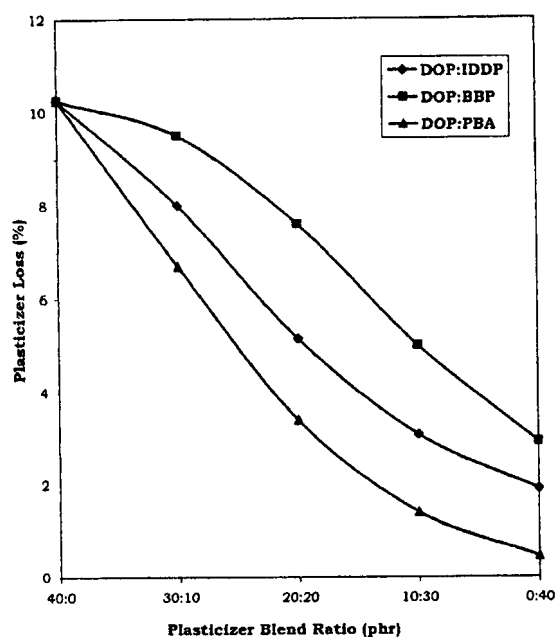


Fig. 5. Leaching of plasticizers from PVC in kerosene at room temperature for 24 h, obtained by systematic replacement of diethylhexyl phthalate (DOP) by isodecylidiphenyl phosphate (IDDP), butylbenzyl phthalate (BBP) or poly(butylene adipate) (PBA) as plasticizers. Reprinted from Ref. [50], © (2003), with permission from John Wiley and Sons, Inc.

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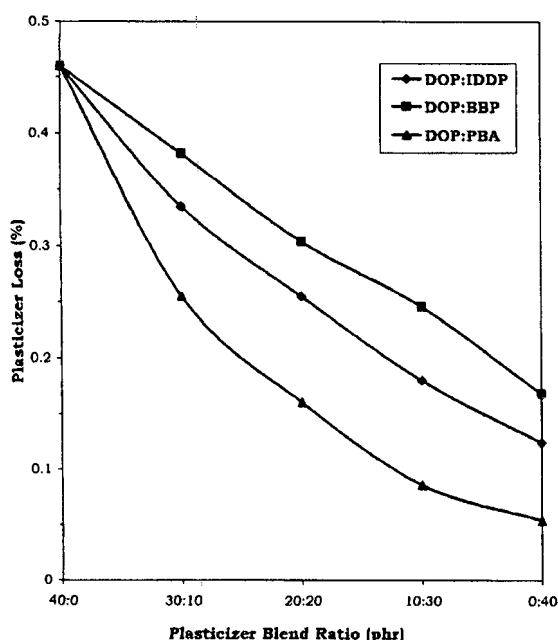


Fig. 6. Solid-migration of plasticizers from 50 mm diameter PVC discs to two 30 ml layers of finely divided silica, obtained by systematic replacement of diethylhexyl phthalate (DOP) by isodecyldiphenyl phosphate (IDDP), butylbenzyl phthalate (BBP) or poly(butylene adipate) (PBA) as plasticizers. Reprinted from Ref. [50], © (2003), with permission from John Wiley and Sons, Inc.

the plasticizer leaching. The smallest oligomers leached out 90-fold more readily than the bulk plasticizer.

While polymeric plasticizers may cause a reduced flexibility in plastic materials, they can also be used in combination with traditional plasticizers to improve leaching resistance of the latter. A terpolymer of ethylene, vinyl acetate and carbon monoxide (EVACO), with reported MW of 240200, was used to plasticize food grade PVC along with DEHA [52]. EVACO was able to reduce the leaching of DEHA, in the organic extractant isooctane, literally to zero. Plasticizers of this type might allow us to prevent leaching of plasticizers as well as formulate plastics with desired mechanical properties.

Polymeric plasticizers and oligomers are now being produced commercially. A wide variety of these plasticizers are available to provide desired properties to different polymers. Manufacturers including P.A.T. Products, Inc., Environmental Protection Inc., and Velsicol Chemical Corp. are engaged in producing low viscosity polymeric plasticizers

and these innovations are being introduced to the current plasticizer market. For example, Bayer Chemicals recently started producing a new polymeric plasticizer, Ultramoll® VP SP 51022, which is a low-viscosity polymeric plasticizer based on phthalic acid [53]. This particular plasticizer is characterized by good migration resistance and high thermal stability. Plastic moldings, cable sheathing and cords with a wide range of hardness and elasticity can be produced using this plasticizer.

4.1.3. Alternative plasticizers

Extensive research is going on to find alternative plasticizers for medical and other commodity plastic materials. Several alternatives have been suggested so far. Some offer better compatibility with polymers, while some show less migration and leaching tendency. However, the toxicological information about many of them are unknown. Also many are expensive and the mechanical properties offered are different than those offered by the traditional plasticizers. So the quest for novel plasticizers continues.

Morflex, Inc., set out to find a suitable, less toxic replacement for DEHP and developed Citroflex® A-6 and Citroflex B-6 based on citric acid esters which are bio-based and biodegradable. Initial toxicity tests conducted by the Pfizer Drug Safety Evaluation Department proved citrates to be safe through acute dermal toxicity and ocular irritation tests in rabbits, and acute oral toxicity tests in mice and rabbits [17]. Also, the citrate-based plasticizers did not induce gene mutation when tested in microbial cells and mammals. However, in later animal studies, citrates were found to cause respiratory irritation, nervous system effects, and effects on blood pressure and calcium metabolism [24]. Tests conducted by Morflex, Inc., showed that Citroflex B-6 was an ideal candidate replacement for DEHP since it provided similar properties to PVC, when combined with ESO [17]. Yet it had poor oil extraction properties compared to DEHP. So, citrates are best suited for medical plastics not exposed to high lipid media. They are being used as plasticizers in packaging and medical devices for years. However, health effects arising from long-term exposure to citrates in medical devices have not been widely studied.

Bayer Chemicals invented phenol alkyl sulfonate plasticizers and is producing them under the trade

name Mesamoll® [54]. These sulfonates have been proven to be effective for a number of polymers including PVC and polyurethanes. This class of plasticizers has outstanding gelling capacity which offers reduced processing time and temperature. Their main advantage is that they have significantly greater saponification resistance than phthalate plasticizers and display a much reduced tendency to leach out, which is particularly important for biomedical plastics exposed to warm, aqueous media for an extended period of time. Also, PVC plasticized with Mesamoll has shown improved tear strength and resistance to weathering and light. These plasticizers are typically used in sealing and adhesive systems, swimming pool covers, shower curtains, rain-wear and in automotive industries.

Ionic liquids (ILs) are a relatively new class of compounds that have been investigated as plasticizers for PVC and poly(methyl methacrylate), PMMA, and were found to be compatible with both the polymer systems [55–57]. Fig. 7 shows the structures of some ILs studied as plasticizers for the abovementioned polymer systems. ILs have already gained wide recognition as potential environmentally-benign solvents [58]. ILs have low volatility, low melting points (as low as -96°C has been reported), a wide (often $\sim 400^{\circ}\text{C}$) liquid range, are high-temperature stable, nonflammable

and are compatible with a wide variety of organic and inorganic materials. It was found that a number of imidazolium-, ammonium- and phosphonium-based ILs are capable of producing flexible PVC as does DEHP [57]. Leaching of plasticizers from 20 wt% plasticized PVC samples to water was studied at 50°C for 5 days [59]. An ammonium-based IL, tetrabutylammonium dioctylsulfosuccinate [tbam^+][doss^-], showed much less leaching tendency than the widely used plasticizer DEHP. In a study of migration of plasticizers, phosphonium- and ammonium-based ILs showed excellent migration resistance. Further research is being conducted to examine the leaching resistance of a wide number of ILs in aqueous and saline solutions, when used as plasticizers in PVC.

4.1.4. Alternative polymers

While many researchers have investigated the approach of using alternative plasticizers to minimize leaching of plasticizers, some researchers have focused on replacing PVC-DEHP systems with alternative polymers. Polyolefins are currently popular because of their ease of processing, low cost and durability [24]. Metallocene polyolefins have been especially popular due to their narrow MW distribution and flexible nature that requires only a small amount of additives. Hence, they are not readily subjected to problems like leaching

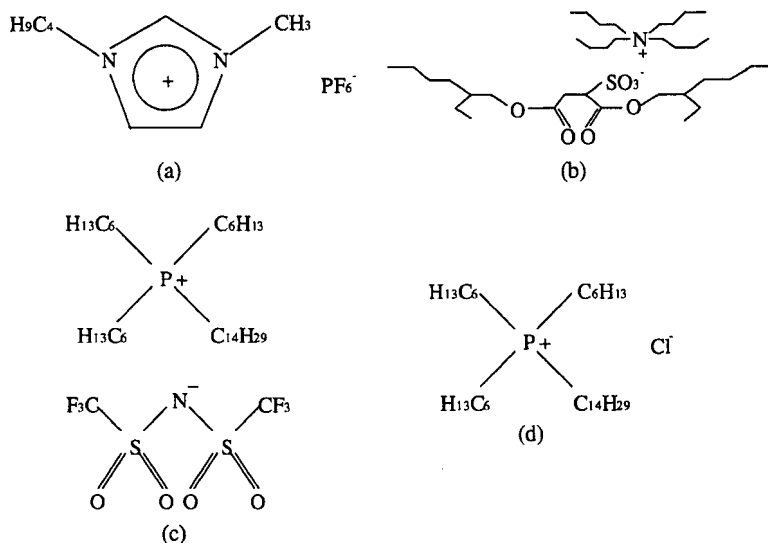


Fig. 7. Structure of some ILs studied as plasticizers for PVC and PMMA: (a) 1-butyl-3-methylimidazolium hexafluorophosphate, (b) tetrabutylammonium dioctylsulfosuccinate, (c) trihexyl(tetradecyl) phosphonium bis(trifluoromethane)sulfonylimide, and (d) trihexyl(tetradecyl) phosphonium chloride.

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and migration. They also produce materials with good mechanical properties. These polyolefins have already started pushing PVC out of the IV bag market. EVA also competes with PVC due to its capability of ranging from a thermoplastic to an elastomeric state depending on the vinyl acetate content in the polymer. It does not need plasticizer and retains its mechanical properties well over time. However, there are instances where the use of PVC plasticized with DEHP is actually favorable and does not need a replacement. For example, in red blood cell storage bags, DEHP has been shown to bind to the cells and stabilize them, extending their shelf life [24]. Polyesters, polyurethane, and silicone are some of the other competing technologies in medical plastics.

4.2. Thermal aging and evaporation of plasticizers

Current research is focused on analyzing the mechanisms of plasticizer evaporation, finding new high temperature stable plasticizers, and implementing measures to inhibit loss of plasticizer at high temperatures. Since some polymers are unstable at elevated temperatures (notably PVC, which begins to degrade above 100 °C) [5], improved plasticizers are not going to be able to impart high temperature stability to every polymer. However, for specialty applications, especially flexible plastics that operate near moving parts or are subjected to rapid extension and contraction cycles, improved plasticizers may offer significant benefits in longer material lifetimes as well as the possibility of working with flexible materials at temperatures well above the range of today's plastics.

Mrklic et al. [60] studied thermal aging DEHP-plasticized PVC systems and suggested that the rate of evaporation of plasticizers can be represented by a linear first order differential equation. Different kinetic parameters were also analyzed. Values of activation energy were found to rise with increasing plasticizer content. Interfacial mass transport in the surrounding medium was detected as the rate-controlling step in the physical process of plasticizer loss. Later on, the same researchers did a comparative study between a number of phthalates and other commercial plasticizers [61]. All of the plasticizers showed the same kinetic behavior earlier observed with DEHP, while Reofos[®], a phosphate plasticizer,

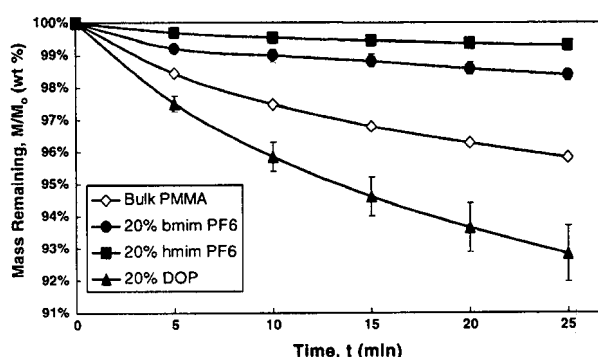


Fig. 8. Short-term thermal stability of bulk PMMA and samples containing 20 wt% 1-butyl-3-methylimidazolium hexafluorophosphate [bmim⁺][PF₆⁻], 20 wt% 1-hexyl-3-methylimidazolium hexafluorophosphate [hmim⁺][PF₆⁻], and 20 wt% di(2-ethylhexyl) phthalate (DOP) at 250 °C. Reprinted from Ref. [56], © (2003), with permission from Elsevier.

showed the highest activation energy barrier to evaporation.

Some new carboxylate esters containing one or more sulfhydryl groups have been found to be remarkably effective as both plasticizers and thermal stabilizers for PVC [62]. These esters function well as primary stabilizers in the absence of metal-containing additives and also lubricate the polymer significantly. In addition to the fact that sulfhydryl groups are effective in removing poisons and toxins, they have the advantage of not having any heavy metal

Table 6

Long-term thermal stability of bulk PMMA and samples plasticized with 1-butyl-3-methylimidazolium hexafluorophosphate [bmim⁺][PF₆⁻] and di(2-ethylhexyl) phthalate (DOP) at 170 °C for 21 days [53]

Plasticizer and content	Sample mass loss (wt% of initial plasticized polymer) (%)	Plasticizer mass loss (wt% of initial plasticizer) ^a (%)
None (bulk PMMA)	2.3	0
10%[bmim ⁺][PF ₆ ⁻]	2.9	8.3
15%[bmim ⁺][PF ₆ ⁻]	3.4	9.6
20%[bmim ⁺][PF ₆ ⁻]	4.6	13.8
30%[bmim ⁺][PF ₆ ⁻]	5.7	13.6
35%[bmim ⁺][PF ₆ ⁻]	6.7	14.9
40%[bmim ⁺][PF ₆ ⁻]	6.9	13.8
20% DOP	15.2	66.8
30% DOP	24.2	75.3

^a Assuming 2.3 wt% of the polymer mass in each sample decomposed at 170 °C.

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component which brings about the debate concerning toxicity of the typical heat stabilizers.

ILs, when studied as plasticizers, were also found to increase the thermal stability of polymers [55,56]. Imidazolium-based hydrophobic ILs were incorporated into PMMA and were found to be compatible with PMMA up to 50 vol% as plasticizers. In addition to lowering the T_g of PMMA ($\sim 120^\circ\text{C}$ when unplasticized) as low as $\sim 20^\circ\text{C}$, and producing polymer samples with mechanical properties similar to those produced by DEHP, the ILs offered far better high temperature stability when compared to DEHP in both short-term (Fig. 8) and long-term (Table 6) experiments. As a plasticizer for PVC, a phosphonium-based IL, trihexyl(tetradecyl) phosphonium bis(trifluoromethane)sulfonylimide, showed superior short-term high temperature stability compared to DEHP [57].

While higher MW polymeric plasticizer PBA was able to produce flexible PVC, it also offered better thermal stability by increasing the onset temperature for degradation when 40 phr DEHP was completely replaced by 40 phr PBA [50].

4.3. Low temperature lubricating plasticizers

Developing new plasticizers that maintain lubricity at temperatures under subzero conditions would provide new materials with reduced low temperature failure, and can be used in such areas as space exploration, and storage of liquefied gases. When more and more plasticizer is added to a polymer, the T_g drops and usually tends to level out when the plasticizer reaches a maximum solubility. But with imidazolium-based ILs as plasticizers for PMMA, the T_g of PMMA showed no sign of leveling out even after being lowered by 100°C from the original value at 50 vol% plasticizer concentration [56]. ILs are known to have melting points as low as -96°C [58] and therefore have the potential to offer satisfactory lubrication to polymers at subzero temperatures.

4.4. Improving health and environmental issues

While point-source pollution can be approached in traditional ways, there are a number of techniques which could help minimizing health and environmental problems owing to the use of leachable plasticizers. One simple way to do this is the use of

alternative flexible polymers (e.g. polyolefins), which require less or no plasticizers [24]. Health and environmental issues can also be improved by reducing the exposure of plasticizers through different surface modification techniques and by using plasticizers that have less volatility and leachability, or by using lower toxicity plasticizers.

4.4.1. Reducing exposure

In Section 4.1, a number of surface modification techniques have been described by which leaching and migration of plasticizers from plastic to adjacent solid, liquid and gaseous media can be reduced. Research to prevent leaching of plasticizers by polar media was instigated by the need for benign biomedical plastics which have less probability of adverse health and environmental effects. Much of the early work on reducing leaching focused on organic extractants, as the plastics were used in various industrial applications. Likewise, early research on biomaterials focused on the biocompatibility of plastic surfaces by minimizing interactions between biomaterial surfaces and biological tissues or blood. Several approaches have been used to enhance the biocompatibility of flexible plastics, especially to prevent protein deposition on plastic surface caused by leaching of DEHP. In the early 1980s, leaching of DEHP during platelet storage in glow discharge-treated and then silicone-coated PVC bags was studied [63]. Glow discharge treatment can introduce different functional groups, cause chain crosslinking or chain scission at the polymer surface. DEHP leaching from PVC bags to blood during platelet storage was reduced from 150 to 200 $\mu\text{g}/\text{ml}/\text{day}$ in untreated PVC to 10–20 $\mu\text{g}/\text{ml}/\text{day}$ in treated PVC bags.

When grafting of PEG on plasticized PVC surface successfully reduced leaching of plasticizer DEHP in three different organic solvents [41], the blood compatibility of the PEG-grafted and ungrafted PVC sheets was evaluated by open-static platelet adhesion studies with platelet rich plasma and this treatment was actually found to reduce the interaction between blood and the polymer surface. The improved blood compatibility of PEG-grafted PVC can be seen in the scanning electron micrographs of platelet adhesion on ungrafted and PEG 4000-grafted PVC sheets (Fig. 9), where the bare PVC surface promoted extensive adhesion of platelets leading to a rough and

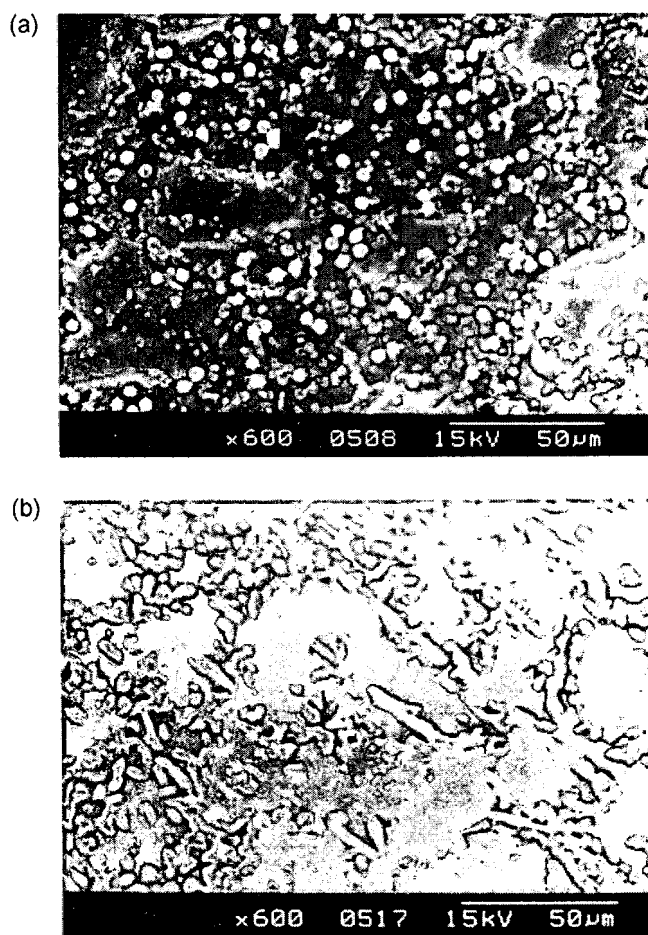


Fig. 9. SEM micrograph of (a) ungrafted and (b) PEG 4000-grafted PVC sheets after being incubated in platelet-rich plasma for 1 h at 37 °C. Reprinted from Ref. [41], © (1998), with permission from Blackwell Publishing Ltd.

nonuniform surface. On the other hand, the plain surface of the PEG 4000-grafted samples is a clear indication of the anticoagulant nature of the graft-modified surface. It was further confirmed by the whole blood clotting time measurements, with ungrafted samples showing much less clotting time compared to the PEG-grafted ones. Grafting PVC with PEG did not alter the mechanical properties of PVC samples in any significant way. Blood compatibility of plasticized PVC was also found to improve with PACVD technique mentioned earlier [44].

Kicheva et al. [34] found that paraffin and complexon coatings can improve the biocompatibility of PVC by providing complete resistance to protein deposition while providing a barrier to DEHP leaching. However, both of these materials have

drawbacks. Complexon coatings are likely to be washed away by flowing blood, while paraffin may crack on bending and therefore is not recommended for long-term use in drain tubes or other biomaterials.

As has already been mentioned, polymeric plasticizers, due to their high MW, have been found to offer good leaching and migration resistance to a number of solvents [48–53], and so did the ILs [59]. These plasticizers have low volatility which also reduces the possibility of off-gassing, thereby reducing the possibility of environmental exposure and offering less health and safety concern regarding plasticizers.

4.4.2. Lower toxicity plasticizers

The use of environmentally-benign plasticizers is another way to improve the health and environmental

issues concerning plasticizers. Among the number of factors that decide the feasibility of a substance to be used as a plasticizer, toxicological information is an increasingly important one. If the plasticizers used have less toxicological effects on living beings, they are obviously less likely to pose health risks upon exposure.

To address the toxicity issue of phthalates, a joint effort by the Ohio Soybean Council and Battelle led to the development of a new plasticizer derived from modified soybean oil [64]. In the past, commercial soybean oil-based plasticizers were not compatible with PVC at the levels needed for primary plasticizers such as phthalates and benzoates. The newly developed environmentally-friendly plasticizer has been found to be fully compatible with PVC, offers more stretching ability than its petroleum-based counterpart, and is also capable of providing high thermal stability unlike many synthetic plasticizers (e.g. DEHP). Being highly effective and based on a renewable agricultural resource, this soy-based plasticizer offers many benefits over existing products. Toxicology and leaching studies are currently in progress.

A new benzoate plasticizer, Benzoflex® 2888 (a blend of diethylene glycol dibenzoate, triethylene glycol dibenzoate, and dipropylene glycol dibenzoate), has been developed by Velsicol Chemical Corporation to account for the leaching problems associated with application of leachable plasticizers in children's toys [65]. Benzoflex has been found to be a good alternative of phthalates as plasticizer when used in flexible toys due to its ease of processing, final product performance, low toxicity and fast biodegradation. Toxicity tests performed according to EU protocols yielded low acute toxicity with an oral LD₅₀ value of 3–5 g/kg in rats, and no evidence of reproductive toxicity. Recent risk assessments conducted by the Toy Manufacturers Association proved the extreme unlikelihood of Benzoflex® 2888 to pose an adverse health risk and therefore it is currently being used in the toy industry.

Toxicity evaluation can be done on whole organisms, with the LD₅₀ values reported for each route of administration (e.g. oral, ocular, transdermal) and species (e.g. mouse, rabbit) tested. More recently, cytotoxicity studies using cell culture instead of whole organisms have been used in screening for the toxicity of materials. For example, Lampen et al. [66] introduced two new in vitro test systems to detect the carcinogenic and teratogenic effect of certain

compounds on mammals. The experimental protocol monitored F9 teratocarcinoma cell differentiation and activation of peroxisome proliferator-activated receptor (PPAR)-ligand-binding domain in the ovary-reporter cells of Chinese hamsters. A series of phthalate esters and their metabolites including two diphthalate and nineteen monophthalate esters were studied. Only five of them were found to induce F9 cell differentiation (or mutagenesis). The same five esters activated the δ type of PPAR (PPAR δ), while most of others activated PPAR α and PPAR γ . Since three of those five esters were already known teratogenic compounds, the combined result of the differentiation and activation assays actually helped detecting possible teratogenic phthalate esters and derivatives. Thus, these two in vitro experiments can be useful as a screening test in the development of new plasticizers.

4.5. Flammability

Knowing that fire hazards concerning plastic materials can be reduced by reducing the flammability of the plasticizers incorporated in the polymers, a number of researchers have tried alternative plasticizers as replacements. A newly developed alkyl diaryl phosphate plasticizer originally marketed by Monsanto Company under the trade name SAN 2148 was studied as a plasticizer for chlorinated PVC (65% Cl) and results were compared to those with DEHP [15]. Two standard flammability parameters were determined: limiting oxygen index (LOI) and smoke density measurement (flaming mode). With the incorporation of equal amounts of either plasticizer, SAN 2148 gave higher LOI and char values. More significantly, SAN 2148 lowered smoke density values in many of the formulations studied. Another benefit of using SAN 2148 as a direct replacement of DEHP is that the phosphate plasticizers appear to stabilize the formulations against thermal decomposition, especially in those systems containing mixtures of flame-retardant and smoke-suppressant.

Another newly developed environmentally-friendly plasticizer, ethylenedioxy-selenophene (EDOS), was studied as an alternative plasticizer to DEHP [67]. PVC was plasticized using either DEHP or EDOS, which is a mixture of 1,3 dioxane derivatives. EDOS matched the ability of DEHP to

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produce flexible PVC, and was less toxic, cheaper and reduced the amount of dioxin-equivalent incineration product formed during burning.

Polymeric plasticizer PBA, which offered good leaching and migration resistance and high temperature stability, also improved the flammability characteristics of PVC by increasing the limiting oxygen index [50]. This was probably due to the higher flash point of the plasticizer used.

ILs represent another viable approach to reduce flammability concern regarding plasticizers. All the commercial plasticizers, even the phosphate esters, are known to lower the LOI of the compound with increasing plasticizer concentration [68]. ILs have been proposed to be flame-retardant plasticizers, because they are known for their nonflammability [58].

4.6. Ultraviolet stability

In many cases, UV stabilizers are added to plastic formulations, but the development of plasticizers that have the added capability to delay or halt UV-induced polymer degradation could minimize the need for stabilizers. Rahman et al. [57] investigated the stability of PVC plasticized with ILs and traditional plasticizers under UV rays at $\lambda=254$ nm. After a short-term (1 min) exposure, sample moduli were increased for all the samples probably due to crosslinking effect. The samples containing trihexyl(tetradecyl) phosphonium bis(trifluoromethane)sulfonylimide, a phosphonium-based IL, as plasticizer went through minimum change in moduli and were able to retain original properties most effectively. Stability of plasticized PVC under UV irradiation of different intensities is currently being studied.

4.7. Plasticizers for biodegradable polymers

One of the most important factors in designing biodegradable polymers is the rate of degradation of the product. A number of plasticizers have been investigated to be used with biodegradable polymers. Citrate plasticizers, being biodegradable esters, gained much attention. PLA, which has been extensively studied in medical implants, suture, and drug delivery systems since the 1980s due to its biodegradability, was plasticized with four

commercially available citrate plasticizers: triethyl, tributyl, acetyltriethyl and acetyltributyl citrate [69]. The plasticizing effects on thermal and mechanical properties of PLA were satisfactory in that the citrate esters produced flexible materials. The high MW citrates also reduced the degradation rate of PLA. However, a considerable amount of plasticizer loss was encountered during processing, especially with the lower MW citrates. Elsewhere, citrate esters were used to plasticize cellulose acetate, and the biodegradation rates increased dramatically with an increase in plasticizer content [70].

Polyols are another class of compounds which have been studied as plasticizers for biodegradable polymers. Glycerol, which is often used with biodegradable polymers, was found to reduce degradation of thermoplastic starch (TPS). Starch, a polysaccharide found abundantly in plants, is not a thermoplastic material itself. But at moderately high temperatures (90–180 °C), under pressure and shear stress, starch granules melt and flow to give an amorphous material called TPS, which can be processed just like a thermoplastic synthetic polymer. The utilization of TPS for the production of biodegradable plastics has increased and has been the object of several studies in the last decade. One of the problems associated with TPS processing is degradation of starch. The effects of glycerol in preventing degradation of TPS, reinforced with cellulosic fibers, were observed [71]. An increase in glycerol content reduced chain degradation considerably. However, an increase in the fiber content amplified it.

In another experimental study, glycerol, ethylene glycol (EG), propylene glycol (PG), diethylene glycol (DEG) and triethylene glycol (TEG) were tested as plasticizers for a biodegradable polymer based on a sunflower protein and aging properties were observed [72]. Films with high-quality mechanical properties were formed which had shear strength similar to that of the low-density polyethylene used in agricultural mulching. They were also sufficiently impermeable to water vapor. An aging study showed that the relatively lighter plasticizers (PG, EG, DEG) were lost over time. However, there was no marked loss of glycerol or TEG over the 3-month aging period. These two plasticizers have the advantage of being suitable for use in the food industry as they are on

the FDA’s Generally Regarded As Safe (GRAS) list. Glycerol was found to be an excellent plasticizer for starch [73] and edible gellan films too [74], while PEG 400 was found to be effective at imparting flexibility to methylcellulose [75].

The group of Boutevin investigated two new amine-based plasticizers for biopolymer films made of wheat gluten, which is used for food-packaging [76]. Glycerol is the most used plasticizer for wheat gluten films. But glycerol causes the film to have high water-vapor permeability and often migrates from gluten films due to its high sensitivity towards moisture. Diethanolamine and triethanolamine were studied as plasticizers which did not change water vapor barrier properties of gluten films, but significantly increased extensibility and elasticity at moderate relative humidity, RH (Table 7). However, at high RH, the effects of plasticizers were overshadowed by the large amount of moisture absorbed by the polymer films.

Tarvainen et al. [77] studied the effectiveness of two *n*-alkenyl succinic anhydrides (ASAs), 2-octenyl succinic anhydride (OSA) and 2-dodecen-1-ylsuccinic anhydride (DYA) as plasticizers for the film-forming polymer ethyl cellulose (EC). OSA is typically used to increase drug dissolution properties of starch and also in the chemical and paper industries, as an oil-phase corrosion inhibitor. The principle of the experiment was to investigate the plasticizing

effectiveness of the long hydrocarbon chains with accessible carbonyl groups. Triethyl citrate (TEC) and dibutyl sebacate were used as reference plasticizers. Due to the excellent mechanical properties (a tough film structure with considerable flexibility) and low permeability of the plasticized films, both the *n*-ASAs, especially OSA, proved to be ideal plasticizers for EC-based coatings at 30 wt% or higher concentrations.

Methylparaben (methyl-*p*-hydroxybenzoate), which is GRAS and is used in the cosmetics industry and as a preservative in the pharmaceuticals industry, was studied as a solid-state plasticizer for a thermally stable pharmaceutical grade acrylic polymer, Eudragit® RS PO, during a hot-melt extrusion process [78]. The *T_g*, melt viscosity and rheological properties of the extrudates containing methylparaben were compared with the extrudates containing traditional plasticizers. It was found that methylparaben was as effective as traditionally used TEC in reducing torque during the extrusion process. Solid state NMR spectra indicated a change in the chemical shift of Eudragit RS PO plasticized with methylparaben, which could be ascribed to an interaction between the hydroxyl group of the methylparaben and the ester group of the Eudragit RS PO polymer. The results of this study demonstrated that methylparaben could be used as a solid-state plasticizer for the Eudragit RS PO

Table 7
Effects of plasticizer concentration and relative humidity on the mechanical properties of gluten films [72]

Plasticizer		σ_R (MPa)	ϵ_R (%)	<i>E</i> (MPa)
Compound	Concentration (g/100 g dm)			
Panel A: results at 58% RHs				
Glycerol	10	12.1(2.3)	4(1)	5.7(1.9)
	20	2.6(1.1)	22(10)	2.6(1.1)
Diethanolamine	10	7.5(2.9)	9(5)	2.3(1.6)
	20	4.1(1.9)	125(8)	0.1(<0.1)
Triethanolamine	10	10.1(1.5)	6(2)	0.1(0.1)
	20	5.3(1.2)	114(8)	0.1(0.1)
Panel B: results at 98% RHs				
Glycerol	10	0.4(0.1)	11(4)	0.1(<0.1)
	20	0.9(0.2)	30(6)	0.1(<0.1)
Diethanolamine	10	1.0(0.1)	61(11)	<0.1(<0.1)
	20	0.8(0.3)	58(11)	<0.1(<0.1)
Triethanolamine	10	1.3(0.9)	103(10)	<0.1(<0.1)
	20	0.8(0.2)	54(9)	<0.1(<0.1)

σ_R , tensile strength at break; ϵ_R , elongation at break; *E*, Young modulus.

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polymer when a hot melt extrusion technique is employed in the preparation of sustained release tablets.

The extensive use of polymers in short-term packaging and disposable applications, and in food and pharmaceutical industries, has stimulated research interest in biodegradable plasticizers as an alternative to the conventional nondegradable ones. This is one of the major research interests in the plasticizer industry now. With the expansion of biodegradable plastic industry, owing to the growing global concern about the environmental impact of persistent plastics, biodegradable plasticizer research continues to grow.

5. Conclusions

Plasticizers form a major part of the plastic industry. The diversified applications of plastics in numerous fields of applications largely depend on the performance of the plasticizers incorporated. In the past century, the plasticizer industry came across a number of technical challenges. Leaching and migration of plasticizers have been reduced by methods including surface crosslinking, grafting, and surface extraction, the use of alternative and novel plasticizers and also the use of alternative polymers which do not require plasticizers. Many of these methods to prevent leaching and migration of plasticizers have been developed on a case-by-case basis, where different methods were successful for particular solvents or plasticizers. Research is being carried out worldwide in both academic and industrial laboratories to provide tunable solutions to the leaching and migration issues. Also, plasticizers are being sought to improve the biocompatibility of flexible plastics since they are widely used in medical applications.

High temperature stable plasticizers are under investigation to provide materials that meet demanding work environments. New and modified plasticizers have also been developed to impart nonflammable properties to polymers. With the extensive growth in the biodegradable polymer market, a major portion of plasticizer research is now focused on materials which are GRAS and are capable of providing flexibility to polymers. As

the plastic industry continues to expand, new challenges arise for the plasticizer industry. Thus, different approaches to resolve the shortcomings of traditional plasticizers for use in a multitude of plastic materials have led to the continuing quest for specialty plasticizers.

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