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Review

Poly(meth)acrylate-based coatings

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ABSTRACT

Poly(meth)acrylate coatings for pharmaceutical applications were introduced in 1955 with the launch of EUDRAGIT® L and EUDRAGIT® S, two types of anionic polymers. Since then, by introducing various monomers into their polymer chains and thus altering their properties, diverse forms with specific characteristics have become available. Today, poly(meth)acrylates function in different parts of the gastrointestinal tract and/or release the drug in a time-controlled manner. This article reviews the properties of various poly(meth)acrylates and discusses formulation issues as well as application possibilities.

Contents

1. Introduction

The success story of poly(meth)acrylates for pharmaceutical coatings began in 1933. That year saw the development of methacrylic acid co-polymer chemistry and the ensuing market launch of Plexiglas® by Röhm and Haas. At the Paris World Exposition in 1937, visitors could view a violin made of Plexiglas®,

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Table 1
Ready-to-use formulations with poly(meth)acrylates.

Name	Polymer	Manufacturer	Application
EUDRAGIT® E PO Ready Mix	Poly(butyl methacrylate-co-(2-dimethylaminoethyl) methacrylate-co-methyl methacrylate) 1:2:1	Biogrund	Protective coatings
Acryl-EZE®	Poly(methacrylic acid-co-ethyl acrylate) 1:1	Colorcon	Enteric coating
Aquapolish® E	Acrylic acid copolymer	Biogrund	Enteric coating
Aquapolish® R	Ammonio methacrylate copolymer (type A and type B)	Biogrund	Sustained release

a crystal-clear unbreakable organic glass of outstanding quality. Since then, the properties of poly(meth)acrylates have been altered for various applications, including for use in pharmaceutical coatings. These are produced by introducing diverse monomers into the polymer chains, thus creating distinct variations with specific characteristics. Trommsdorff and Grimm, for example, described enteric coatings for solid dosage forms in a patent application in 1952. Today, poly(meth)acrylates function in different parts of the gastrointestinal tract and/or release the drug in a time-controlled manner.

In 1955, the first poly(meth)acrylates for pH-controlled release became commercially available (EUDRAGIT® L and EUDRAGIT® S as organic solutions in isopropyl alcohol). These were followed in 1959 by those intended for immediate-release applications (EUDRAGIT® E). Only ten years later poly(meth)acrylates for time-controlled drug release were launched. With growing environmental and safety concerns, aqueous polymer dispersions were developed and marketed in 1972 to replace organic coating solutions. Over the years, numerous oral dosage forms using poly(meth)acrylate coatings have been introduced, employing not only simple coatings but also combining poly(meth)acrylates to achieve specific release profiles. Advances have included innovative formulations as well as new technologies in product development. One example is ready-to-use polymer mixtures combined with color matching possibilities, which are quicker to prepare and allow customization. These types of polymer systems contain all the necessary excipients in a powder mixture that only needs to be stirred into a solution prior to coating.

Ready-to-use products are listed in Table 1.

2. Poly(meth)acrylates

Poly(meth)acrylates are synthetic (co)polymers prepared by free-radical polymerization. They exhibit extremely low batch-to-batch variations when compared to natural, raw material polymers. Synthetic polymers have very narrow specifications due to their excellent reproducibility and are monographed in the European Pharmacopoeia, the USP/NF and the Japanese Pharmaceutical Excipients. Drug master files for the entire range exist at the US Food and Drug Administration (FDA). Poly(meth)acrylates are available in different forms: as aqueous dispersions, organic solutions, granules or powders. Their physicochemical properties are determined by functional groups, and their solubility in the digestive tract results from monomer variations and polymerization reaction. Acidic or alkaline groups of soluble poly(meth)acrylates enable pH-dependent release through salt formation. Insoluble but permeable cationic or neutral (co)polymers, by contrast, enable delayed release applications through pH-independent swelling and diffusion-controlled dissolution. Due to their excellent film-forming properties (supported by high flexibility, low water vapor transition rates and high pigment uptake) their main application in the pharmaceutical industry is to achieve therapeutically necessary release profiles or to protect the drug from surrounding influences such as humidity or light. Furthermore, they are often used to avoid interactions between film and core as well as to increase patient compliance, e.g. through sustained-release coatings or as a cosmetic improvement. The polymers themselves are pharmacologically inactive and are compatible with skin and mucosal membranes.

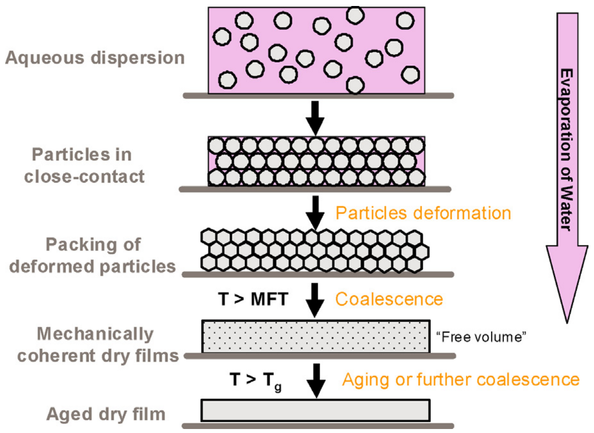

Fig. 1. Film formation mechanism from aqueous dispersions (Hofmann and Stahl, 2012).

3. Properties and coating composition

3.1. Film formation

Besides the polymer and the dispersing or dissolving medium (organic solvents or water), poly(meth)acrylate coating formulations can contain several additives such as surfactants, plasticizers, glidants and pigments. In order to select the appropriate coating excipients, an understanding of the mechanisms behind film formation is necessary. There is a fundamental difference in film-formation between aqueous polymer dispersions, where the polymer and the liquid phase are in a heterogeneous system, and polymer solutions, where the polymer and the liquid phase are in a homogeneous system.

Whereas film formation from a solution simply occurs upon solvent evaporation (sol to gel transition), film formation from aqueous dispersions is more complex (Fig. 1). Here, minimum film-forming temperature (MFT) and glass transition temperature (Tg) are key parameters for efficient film formation. The MFT is the temperature above which a continuous film is formed under defined drying conditions. Upon drying, the particles come into direct contact with each other and form dense sphere packaging, due to evaporation and the surface tension between water and polymer. During further evaporation, capillary forces lead to coalescence of the particles and the forming of a homogeneous film. Coalescence only occurs at temperatures above MFT. To achieve fast film formation, the temperature should be 10–20 K above MFT.

The glass transition temperature is the temperature at which matter changes from a glassy state to a more rubbery state. During this transition, mobility of the polymer chains is increased (Jones, 2007). When films are stored above the Tg, aging or further coalescence can occur and the free volume in the polymer film is reduced. This leads to lower permeability of the film, which