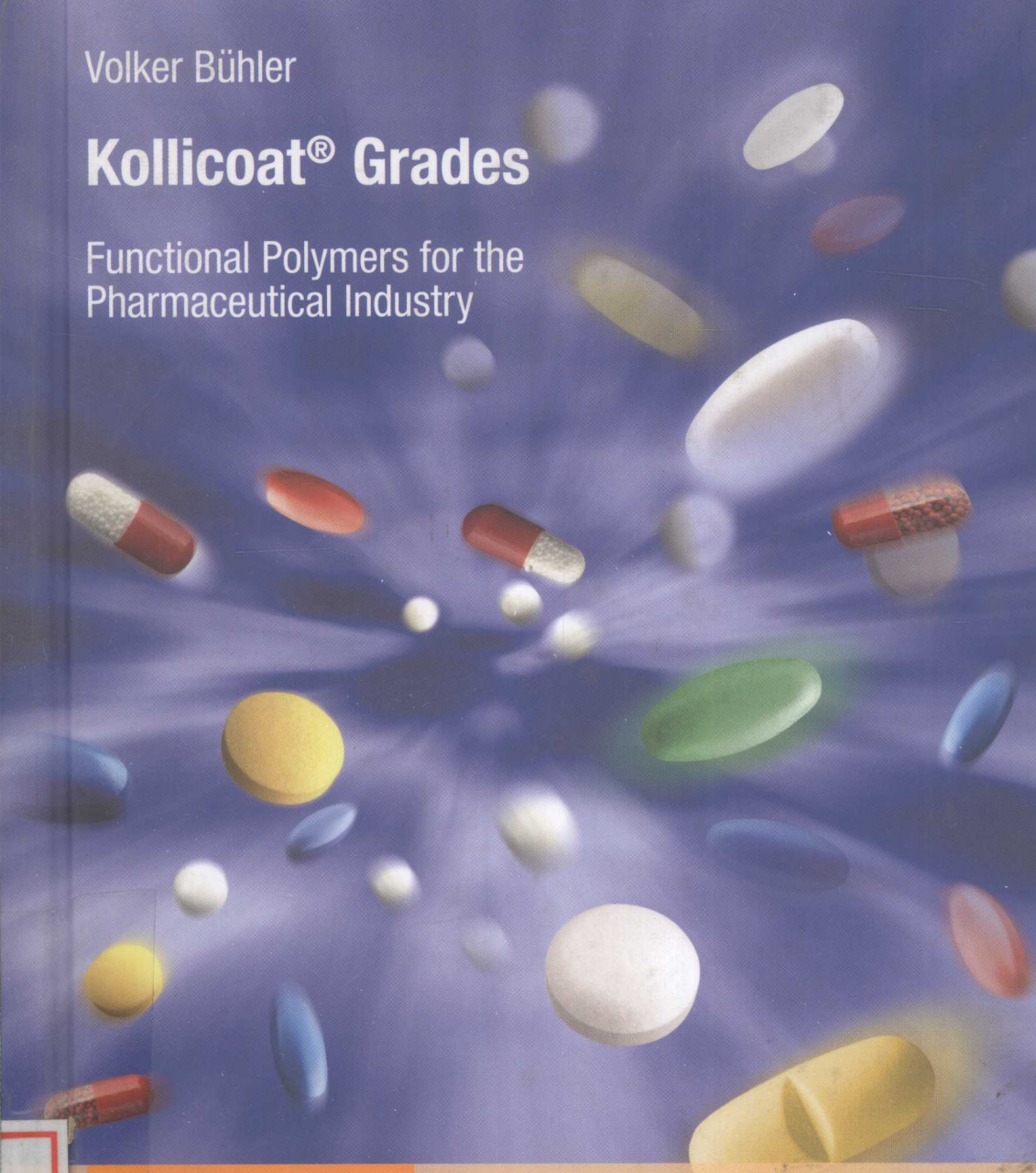
Volker Bühler

Kollicoat® Grades

Functional Polymers for the Pharmaceutical Industry



BASF

The Chemical Company

Volker Bühler

Kollicoat grades

Functional polymers for the pharmaceutical industry

BASF Aktiengesellschaft
Pharma Solutions
67056 Ludwigshafen, Germany

BASF
The Chemical Company

Januar 2007

Dr. Volker Bühler
In den Weingärten 14 · 67157 Wachenheim/Weinstrasse · Germany

Translation:
James Brawley · Scheffelweg 6 · 69251 Gaiberg · Germany

Photo on page 185 courtesy of IMA Industria Macchine Automatiche S.p.A., Bologna, Italy

Registered trademarks in this book

Trademark	Company	Mentioned in chapter
Kollicoat®	BASF	Titelseiten usw.
Kollidon®	BASF	2.1.2, 2.2.6, 2.2.8.4, 2.2.9.1, 2.3.2.3, 2.3.2.4, 2.3.3.2 (5x), 2.3.3.3 (5x), 2.4.1, 2.4.3.2, 2.4.3.3 (2x), 2.5.1, 2.5.3.2 (2x), 3.2.7.2 (2x), 3.3.1 (2x), 3.3.2.1, 3.3.2.3 (2x), 3.3.3.1 (3x), 4.1.1 (2x), 4.2.2, 4.3.1 (3x), 4.3.2.4 (6x), 4.3.3.2 (4x), 4.3.4.2, 4.3.4.4 (3x), 4.3.4.5, 4.3.5.1 (2x), 4.3.6.1 (6x), 4.3.6.2 (6x), 4.3.6.3 (16x), 5.3.1 (2x), 5.3.2.1, 5.3.2.2 (3x), 5.3.2.3, 5.3.2.4 (3x), 5.3.2.5 (3x), 5.3.4.1 (2x), 5.3.4.2 (4x), 6.1, 6.3.3, 6.3.4
Ludipress®	BASF	2.3.2.3, 2.3.2.4, 2.4.3.1, 2.4.3.2, 2.4.3.3, 2.5.3.1, 2.5.3.2, 2.5.3.3, 3.3.2.1, 3.3.2.2, 3.3.2.3, 4.3.2.5 (2x), 4.3.5.1, 5.3.1, 5.3.3.1
Lutrol®	BASF	3.3.1
Cremophor®	BASF	3.3.1
Soluphor®	BASF	4.2.7.2 (2x)
Sivovit®	BASF	2.5.3.2, 3.3.2.1, 3.3.3.2, 4.3.3.2, 4.3.4.4, 5.3.2.2, 5.3.2.4, 5.3.2.5
Ascorbinsäure C97™	BASF	2.4.3.3, 2.5.3.2
Accela Cota®	Manesty	2.3.2.4 (2x), 2.3.2.6 (3x), 2.4.3.1 (2x), 2.5.3.1 (2x), 2.5.3.3 (2x), 3.3.2.1 (2x), 3.3.2.2, 3.3.2.3, 3.3.4 (2x), 4.3.3.2 (2x)
Driacoater®	Driam	2.3.2.3 (2x), 2.3.2.6 (2x), 2.4.3.2 (2x)
Sepispers®	Seppic	2.4.2
Hi-Coater®	Freund Industrial	2.4.3.3 (2x), 2.5.3.2
Labrasol®	Gattefossé	2.5.2
Aerosil®	Degussa	2.5.3.3, 3.3.2.3, 4.3.2.2 (2x), 4.3.2.3 (2x), 4.3.2.4 (2x), 4.3.3.2, 5.3.2.4, 5.3.2.5, 5.3.3.2 (2x), 5.3.3.3 (2x), 5.3.5
Aeromatic Strea-1™	Niro	3.3.3.2 (2x), 4.3.2.2, 4.3.2.3, 4.3.2.4, 4.3.2.5, 4.3.4.2 (2x), 4.3.4.4 (2x), 4.3.4.5 (2x), 4.3.6.2, 4.3.6.3, 5.3.2.1 (2x), 5.3.2.3 (2x), 5.3.3.2, 5.3.4.2 (2x)
Methocel®	Colorcon	4.3.2.1
Aquacoat®	FMC	4.3.5.1
Karion®	Merck	4.3.6.2, 4.3.6.3
Pharsil®	Wacker Chemie	5.3.1, 5.3.2.1

Contents

Preface

BASF offers a full range of aqueous film coating materials covering a broad pharmaceutical application spectrum ranging from instant release (e.g., moisture protection, taste masking) to modified release (e.g., enteric- and sustained release) coatings under the brand name Kollicoat. This book provides a comprehensive description of the properties and applications of the different Kollicoat grades.

Chapter 1 gives a brief introduction to the different Kollicoat product grades, especially to their classification/composition and fields of application. Each of the following 4 chapters reviews one of the four available Kollicoat product groups.

The Kollicoat IR film formers are water-soluble and are based on PEG-PVA copolymers and various additives. They can be used as instant release coatings (e.g., taste masking, moisture-and oxygen protection), as binders for wet granulation, as hydrophilic pore formers in sustained release coatings and as stabilisers in suspensions. The two Kollicoat MAE grades (based on methacrylic acid-ethyl acrylate copolymers) are for enteric coatings and are available as an aqueous dispersion or powder respectively.
Kollicoat SR 30D is an aqueous dispersion of poly(vinyl acetate). It is used primarily for sustained release coatings, but can also be used as a granulation fluid for matrix tablets. Kollicoat EMM 30D is an aqueous dispersion of ethyl acrylate-methyl methacrylate copolymer and is used as a sustained release coating or granulation material. The chapters on the different Kollicoat grades are similarly structured and thus make for ease of reading. They list in great detail the chemical structure/composition, product specifications, extensive product properties [e.g., solubility, dissolution behaviour, dispersibility, viscosity, hygroscopicity, powder properties (particle size, bulk density)], film properties (mechanical properties, dissolution, tackiness, permeability), stability on storage and detailed formulation and process examples (e.g. preparation of coating formulations, coating equipment process parameters (small scale and scale-up), and product characterization).

In chapter 6, valuable practical advice for film coating with the Kollicoat excipients is provided. The effect of coating process parameters (e.g., air temperature and volume, spray rates/pressure, nozzle settings, etc.) and formulation variables (e.g., viscosity/solid content of spray formulation, effect of plasticizers, pigments, etc.) and their adjustments to achieve the desired product properties or to solve processing and product problems are described in detail. Finally, chapter 7 gives an overview of toxicological studies, pharmacopoeial monographs and the registration status of the Kollicoat grades.

This book provides scientists with a clear and extensive guide on the use of the Kollicoat grades for both instant and modified release applications. Numerous examples with detailed formulation and process information aid the formulator in his task of quickly developing high-quality pharmaceutical dosage forms.

Prof. Dr. R. Bodmeier
College of Pharmacy
Freie Universität Berlin

1. Introduction and product overview

The Kollicoat range of products comprises seven modern high-quality film-forming agents that are used in the pharmaceutical industry for the production of medicinal products. They can be divided into four groups, each of which has a different chemical structure designed for the applications intended. With the exception of the Kollicoat MAE grades, they are all neutral, based on various homo-, co- or graft polymers. The Kollicoat MAE grades are ionic co-polymers. An overview of the basic chemical structures involved is given in Table 1 below.
The names given to the individual products do not always have a common origin. In the case of the Kollicoat IR and SR grades, the designations "IR"(Instant Release) and "SR" (Sustained Release) refer to specific applications. In the case of the acrylate copolymers Kollicoat MAE and EMM, the letters refer to the specific monomers used.

Table 1: Kollicoat product groups and their chemical structures

Product group	Basic chemical structure	Monomers
Kollicoat IR	Graft polymer, neutral	Ethylene oxide, vinyl acetate, saponified
Kollicoat MAE	Copolymer, ionic	Ethyl acrylate, methacrylic acid
Kollicoat SR	Homopolymer, neutral	Vinyl acetate
Kollicoat EMM	Copolymer, neutral	Ethyl acetate, methyl methacrylate

The Kollicoat grades have a very wide range of applications. These range from simple water-soluble tablet coatings, gastric juice-resistant films, sustained-release matrix forms to film-formers in sprays. Table 2 gives a rough overview of the most important applications. Additional details and examples of formulations are given in the appropriate chapters dealing with the specific Kollicoat types.

Table 2: Main application areas of the Kollicoat grades

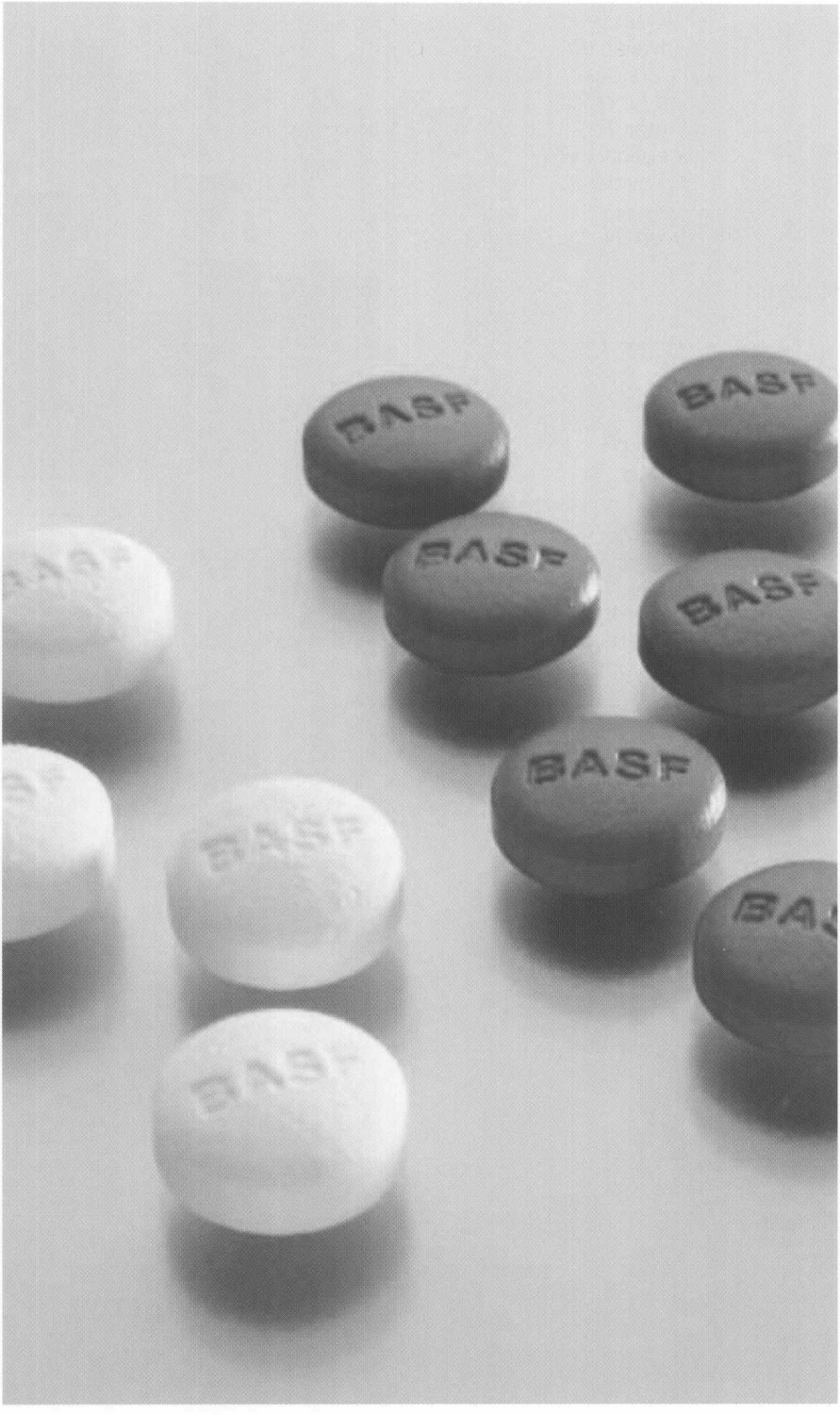
Product group	Principal application areas
Kollicoat IR	White or coloured, water-soluble and protective tablet coatings
Kollicoat MAE	Enteric coatings for tablets, capsules and crystals/ granules
Kollicoat SR	Sustained release polymer for tablets, sustained release coatings for pellets, taste masking in tablets
Kollicoat EMM	Sustained release coatings for pellets, sustained release polymer for tablets

The various Kollicoat grades available are adapted to the application in question. Some are available as powdered polymer, others as blends and others as aqueous dispersions. As all the products are intended for processing in water, only those types are in powder form that can be readily dissolved or suspended in water. Ready-made suspensions facilitate use in the production of pharmaceuticals. Powdered forms on the other hand can be stored longer. Table 3 provides an overview of the available types.

Table 3: The seven available Kollicoat grades

Product	**Powder polymer**	**Coating blend in powdered form**	**Aqueous dispersion**
Kollicoat IR	+		
Kollicoat IR White		+	
Kollicoat Protect		+	
Kollicoat MAE 30 DP			+
Kollicoat MAE 100P	+		
Kollicoat SR 30 D			+
Kollicoat EMM 30 D			+

The applications for the various Kollicoat grades are described in this book using formulations that have been developed in the Application Laboratories of BASF AG or in cooperation with these laboratories.


BASF
BASF
BASF
BASF
BASF
BASF
BASF

2. Kollicoat IR grades

2.1 Product range, structure, packaging

2.1.1 Product range

The Kollicoat IR product range comprises three individual types differing mainly in composition. Kollicoat IR is a pure polymer; Kollicoat IR White is a ready-made mixture for direct use based on Kollicoat IR; and Kollicoat Protect is a mixture of Kollicoat IR and a further well-known polymer as film-forming agent. All three products are listed in Table 4 with their BASF article and substance (PBG) numbers.

Manufacture of all three products is according to cGMP.

Table 4: Kollicoat IR grades

Product	BASF article number	PBG number
Kollicoat IR	55554797 (20 kg)	10219929
Kollicoat IR White	56653329 (30 kg)	10581609
Kollicoat Protect	56654018 (20 kg)	10581610

2.1.2 Chemical structure and composition

Kollicoat IR

Kollicoat IR powder comprises polyethylene glycol and polyvinyl alcohol bound in the ratio of 25:75. A polyethylene glycol chain forms a base onto which side chains of polyvinyl alcohol are grafted. The mean molecular weight is approximately 45,000. The precise structure is shown in Fig. 1. Kollicoat IR is manufactured in Ludwigshafen, Germany. The polyvinyl alcohol side chains are produced by grafting the vinyl acetate monomer onto the polyethylene glycol chain, which is then saponified. The product is subsequently spray-dried, 0.3 % silica gel being added as a flowability agent.

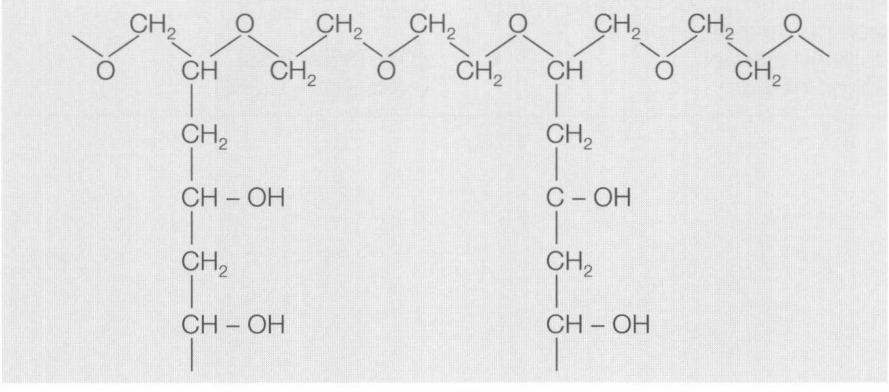


Fig. 1: Chemical structure of Kollicoat IR

Kollicoat IR White

Kollicoat IR White is a ready-mix powder comprising the two film-forming agents Kollicoat IR and copovidone [3], the pigments titanium dioxide and kaolin and the stabiliser sodium lauryl sulphate. It is available for direct use as a white soluble tablet or capsule coating. White coatings play a more important role that would appear at first glance. In 2004 in Germany, for example, they had a market share of approximately 40 %.
The precise composition of Kollicoat IR White is shown in Table 5. Due to the use of innovative technology, the insoluble components titanium dioxide and kaolin are embedded in the polymer matrix in such a way that, when the powder is subjected to mechanical stress, they neither separate physically nor do they agglomerate.

Table 5: Composition of Kollicoat IR White

Components	Content	
Kollicoat IR	61.2 %	(45 – 74 %)
Copovidone (Kollidon VA64)	6.8 %	(5 – 10 %)
Titanium dioxide	14.0 %	(10 – 20 %)
Kaolin	16.0 %	(10 – 20 %)
Sodium lauryl sulphate	2.0 %	(1 – 5 %)

Kollicoat Protect

Kollicoat Protect is a mixture of Kollicoat IR and polyvinyl alcohol, the latter having a mean molecular weight of approximately 30,000 (Table 6). Both components are mixed in solution form during manufacture and dried in such a way that a powder mix consisting of uniform particles is formed that does not allow the components to separate when subjected to mechanical stress.

Table 6: Composition of Kollicoat Protect

Components	Content
Polyethylene glycol-polyvinyl alcohol graft polymer (Kollicoat IR)	60 % (55 – 65 %)
Polyvinyl alcohol	40 % (35 – 45 %)
Silicon dioxide	0.3 % (0.1 – 0.3 %)