CONTACT LENSES

Materials, Chemicals, Methods and Applications

Johannes Karl Fink

Scrivener Publishing

WILEY

Contact Lenses

Scrivener Publishing
100 Cummings Center, Suite 541J
Beverly, MA 01915-6106

Publishers at Scrivener
Martin Scrivener (martin@scrivenerpublishing.com)
Phillip Carmical (pcarmical@scrivenerpublishing.com)

Contact Lenses

Materials, Chemicals, Methods and Applications

Johannes Karl Fink
Montanuniversität Leoben, Austria

WILEY

This edition first published 2022 by John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA and Scrivener Publishing LLC, 100 Cummings Center, Suite 541J, Beverly, MA 01915, USA

For more information about Scrivener publications please visit www.scrivenerpublishing.com.

Wiley Global Headquarters
111 River Street, Hoboken, NJ 07030, USA

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Library of Congress Cataloging-in-Publication Data

ISBN 978-1-119-85735-8

Cover image: Pixabay.com
Cover design by Russell Richardson

Set in size of 11pt and Minion Pro by Manila Typesetting Company, Makati, Philippines

Printed in the USA

10 9 8 7 6 5 4 3 2 1

Contents

Preface

This book focuses on the chemistry and properties of contact lenses and their fabrication methods.

The text starts with a chapter in which a detailed history of contact lenses spanning over almost 500 years is presented

Next, common materials that are used for the fabrication of contact lenses are listed and explained, including both the monomers and polymers that are used in their production. Special issues regarding soft lenses, clear contact lenses, and functional contact lenses are also discussed.

Functional contact lenses can be used for remote health monitoring and ocular drug delivery systems. Besides the materials used here, these issues are detailed in further separate chapters. Also, special fabrication methods are discussed, e.g., the fabrication of multifocal contact lenses and the fabrication of ultrathin coatings.

There is also an important discussion on additives that can be used, e.g., for oxygen-permeable materials or anti-biofouling materials.

The chapter ends with a discussion of simulation methods for contact lenes, such asocular topography parameters, gas-permeable lenses, and computerized videokeratography.

In the second chapter, several common fabrication methods for contact lenses are discussed. Here, computer-aided contact lens design, methods for the fabrication of colored contact lenses, and the fabrication of decentered contact lenses are detailed.

Also, special processes are reviewed, including mold processes, reactive ion etching, electrospinning and others.

Another chapter discusses the properties of contact lenses and methods of measurement. Here, a lot of standard methods are discussed. Besides standard methods, other issues are discussed such as the assessment of cytotoxic effects, the Schirmer tear test and others.

A chapter is devoted to drug delivery of contact lenses, a comparatively new issue.

Finally, a chapter details the possible medical problems related to contact lenses and how to avoid them. These are eye diseases, allergic and toxic reactions. Also, disinfection agents that can be used and methods for the medical treatment of such problems are detailed.

The text focuses on the literature of the past decade. Beyond education, this book will serve the needs of industry engineers and specialists who have only a passing knowledge of the plastics and composites industries but need to know more.

How to Use This Book

Utmost care has been taken to present reliable data. Because of the vast variety of material presented here, however, the text cannot be complete in all aspects, and it is recommended that the reader study the original literature for more complete information.

The reader should be aware that mostly US patents have been cited where available, but not the corresponding equivalent patents in other countries. For this reason, the author cannot assume responsibility for the completeness, validity or consequences of the use of the material presented herein. Every attempt has been made to identify trademarks; however, there were some that the author was unable to locate.

Index

There are three indices: an index of acronyms, an index ofchemicals, and a general index.

In the index of chemicals, compounds that occur extensively, e.g., "acetone," are not included at every occurrence, but rather when they appear in an important context.

Acknowledgements

I am indebted to our university librarians, Dr. Christian Hasenhüttl, Margit Keshmiri, Friedrich Scheer, Christian Slamenik, Renate Tschabuschnig, and Elisabeth Groß for their support in literature acquisition. I also want to express my gratitude to all the scientists who have carefully published their results concerning the topics dealt with herein. This book could not have been otherwise compiled.

In addition, I am very grateful to the ophthalmologists Dr. Anna Schlanitz-Bolldorf and Dr. Ferdinand Schlanitz, who inspired me to write

this text. Last, but not least, I want to thank the publisher, Martin Scrivener, for his abiding interest and help in the preparation of the text. In addition, my thanks go to Jean Markovic, who made the final copyedit with utmost care.

Johannes Fink
Leoben, December 2, 2021

1

Types of Lenses

1.1 History of Contact Lenses

A history of contact lenses spanning over almost 500 years has been detailed (1, 2). It is based on historical works, scientific papers and journal articles and looks at both the modern disposable lens as well as the hard and soft lenses that came before. Some important events are collected in Table 1.1.

Table 1.1 History of contact lenses (2).

Year	Inventor	Issue
1508	Leonardo da Vinci	Corneal neutralization
1637	René Descartes	Fluid-filled tube
1685	Philippe de La Hire	Neutralization of cornea
1801	Thomas Young	Three color theory of perception
1827	George Biddell	Theory of astigmatism
1845	Sir John F. W. Herschel	Convex lenses
1846	Carl Zeiss	Optical instruments
1851	Johann Nepomuk Czermak	Water-filled goggle
1887	Adolf Eugen Fick	First successful contact lens
1961	Otto Wichterle	Soft contact lenses
1979	Kyoichi Tanaka	Silicone hydrogel materials

In 1508, Leonardo da Vinci first had the idea of placing a corrective lens directly onto the surface of the eye (3–5). In 1637, René Descartes proposed another idea in which a glass tube filled with liquid is placed in direct contact with the cornea.

In 1887, Adolf Eugen Fick, a German physiologist, created the first successful contact lens (6). Glass-blown scleral lenses remained the only form of contact lens until 1938, when poly(methyl methacrylate) (PMMA) was developed, and Mullen and Obring used the plastic to manufacture scleral lenses. Obring developed the Plexiglass series in New York in 1940 (4).

In 1961, the Czech chemist Otto Wichterle invented soft contact lenses (7, 8). In 1970, rigid gas-permeable contact lenses were developed, and widely accepted for the advantages of small diameter (about 9 *mm*) and gas permeability. Silicone hydrogel materials were developed in 1979 (9). In 1999, an important development was the launch of the first silicone hydrogels onto the market. These new materials showed an extremely high oxygen permeability with comfort performance (4).

The factors that influenced the development of special materials have been reported (10). Accounts of early attempts to improve vision by use of a lens contacting the eye are limited to a few isolated observations (11). Practical success was not realized until techniques for fabrication of lenses from glass were sufficiently developed (12). PMMA replaced glass in the late 1930s. This material is more durable, more readily fabricated and was claimed by some authors to show a better ocular compatibility (13). During the same broad period of time, there was also a change in emphasis from scleral to corneal contact lenses, which placed different demands on material design and development.

More is demanded from ophthalmic treatments using contact lenses, which are currently used by over 125 million people around the world (14). Improving the material of contact lenses is currently a rapidly evolving discipline (10).

A search has been performed of the titles of papers in the Scopus database to identify contact lens-related articles published this century (15). The ten most highly cited papers were determined from the total list of 4,164 papers found. Rank-order lists by count were assembled for the *top 25* in each of four categories: authors, institutions, countries and journals. A 20-year subject-specific contact lens h-index was derived for each author, institution, country and journal to serve as a measure of impact in the field. The top 10 constituents (of the top 25) of each category were ranked and tabulated (15).

1.2 Materials

Contact lens materials (10) are typically based on polymer- or silicone-hydrogel, with additional manufacturing technologies employed to produce the final lens. These processes are simply not enough to meet the increasing demands for contact lenses and the ever-increasing number of contact lens users (14).

An advanced perspective on contact lens materials has been presented, with an emphasis on materials science employed in developing new contact lenses (14, 16). The future trends for contact lens materials are to graft, incapsulate, or modify the classic contact lens material structure to provide new or improved functionality. Also, some of the fundamental material properties are discussed, and the outlook for related emerging biomaterials is presented.

Contact lens materials and lens types, treatment for contact lens and tear film complications, and myopia correction and contact lenses for abnormal ocular conditions have been detailed (17). Current topics in this field are miniscleral lenses, keratoconus, corneal crosslinking, and pediatric, cosmetic and prosthetic contact lenses. Furthermore, simulation programs for scleral lens fitting, sagittal values, soft toric mislocation, front vertex power, orthokeratology and rigid lens design are discussed.

1.3 Monomers

The monomers that can be used for contact lenses, which are described in the following sections and in both tables and references, are collected in Table 1.2.

These issues will be detailed in the following sections of this chapter.

1.3.1 Monomers for Block Copolymers

A block copolymer that contains both hydrophobic and hydrophilic blocks with amino acid groups has been described (18).

The principal monomers for such block copolymers are a combination of two monomers capable of forming a hydrogel; such monomers are collected in Table 1.3.

Table 1.2 Monomers for contact lenses.

Monomers and monomer types	Usage	References
2-Hydroxyethyl methyacrylate *N*-Vinyl-2-pyrrolidone Methyl methacrylate Isobornyl methacrylate *tert*-Butylcyclohexyl methacrylate	Soft lenses	(19)
Hydrophobic monomers	Strengthening agents	Table 1.8
Hydrophilic monomers		Table 1.8
Hydrophilic monomers	Hydrogels	Table 1.10
Azlactones	Surface treatment	Table 1.12
Acrylamide *N*-Hydroxyethyl acrylamide *N*-Isopropyl acrylamide 2-Acrylamido-2-methylpropanesulfonic acid 2-Hydroxyethyl methacrylate 2-Hydroxyethyl acrylate	Macromers	(20)
Acryl monomers	Water absorbable	Table 1.16
Poly(siloxane)	Water absorbable	Table 1.17
4-(Phenyldiazenyl) phenyl methacrylate	Blue-light blocking	(21)
Acrylates	UV-blocking	Table 1.22
Silicone hydrogel	Multifocal lenses	Table 1.23
Acrylates	Non-silicone hydrogel	Table 1.25
Crosslinking agents	Non-silicone hydrogel	Table Table 1.26
Oxyperm	Oxygen permeable	Table 1.32
Ionoperm	Oxygen permeable	Table 1.32

Table 1.3 Monomers (18).

Monomer	Monomer
2-Ethylphenoxy acrylate	2-Ethylphenoxy methacrylate
2-Ethylthiophenyl acrylate	2-Ethylthiophenyl methacrylate
2-Ethylaminophenyl acrylate	2-Ethylaminophenyl methacrylate
Phenyl acrylate	Phenyl methacrylate
Benzyl acrylate	Benzyl methacrylate
2-Phenylethyl acrylate	2-Phenylethyl methacrylate
3-Phenylpropyl acrylate	3-Phenylpropyl methacrylate
3-Propylphenoxy acrylate	3-Propylphenoxy methacrylate
4-Butylphenoxy acrylate	4-Butylphenoxy methacrylate
4-Phenylbutyl acrylate	4-Phenylbutyl methacrylate

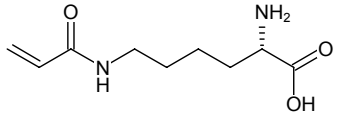
Side-chain-linked amino acids are collected in Table 1.4. Some of these compounds are shown in Figure 1.1.

Table 1.4 Side-chain-linked amino acids (18).

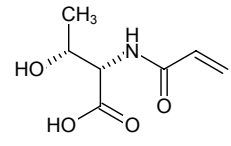
Monomer	Monomer
Acryloyl-*L*-lysine	Acryloyl-*L*-serine
Acryloyl-*L*-threonine	Acryloyl-*L*-tyrosine
Acryloyl-*L*-amino-phenylalanine	Acryloyl-*L*-cysteine
Acryloyl-*L*-oxy-proline	Nϵ-acryloyl-Nα-Oelityl-L-Lysine

The synthesis of a variety of such monomers has been detailed (18). For example, the synthesis of (*S*)-6-acrylamido-2-aminohexanoic acid monomers is performed via a copper complex (18):

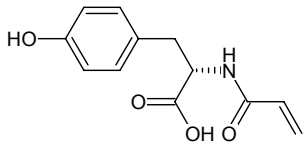
Preparation 1–1: L-lysine (14.62 *g*; 100 *mmol*) was dissolved in 150 *ml* deionized water and heated to about 80°C. Copper carbonate (16.6 *g*; 75 *mmol*) was added in portions over a period of 30 *min*. The reaction was stirred for an additional 30 *min*. The hot, deep-blue suspension was filtered through silica gel. The filter was washed with a small amount of water. On the following day, the lysine copper complex containing the combined filtrate was cooled in an ice bath, and 100 *ml* tetrahydrofuran was added. A solution of acryloyl chloride in methyl-*tert*-butylether (8.9 *ml*, 110 *mmol*) was added dropwise during a period of 1 *h*. The pH was initially maintained between 8 and 10 by parallel, dropwise addition of 10% sodium hydroxide solution. After half of the acryloyl chloride solution had been added, the product began to precipitate. When most of the acryloyl chloride had been added, addition of sodium hydroxide was



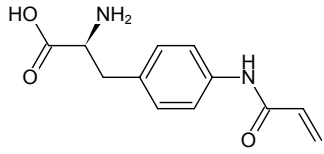
Acryloyl-*L*-lysine



Acryloyl-*L*-threonine



Acryloyl-*L*-tyrosine



Acryloyl-*L*-amino-phenylalanine

Figure 1.1 Monomers for side-chain-linked amino acids.

slowed down to allow the pH to drop to about 6 and the temperature of the reaction mixture was allowed to reach room temperature. The blue suspension was stirred for an additional 2 *h* and was then filtered. The solid material retained on the filter was washed with water and acetone and then dried. A yield of 6.5 *g* of acryloyl-*L*-lysine copper complex was obtained. Acryloyl-*L*-lysine copper complex (29.5 *g*) was suspended in 300 *ml* deionized water and cooled in an ice bath. H_2S gas was bubbled into the suspension until copper sulfide precipitation was complete; then 3 *g* of active charcoal was added to the suspension. The suspension was heated briefly to 100°C. After cooling to room temperature, 500 *ml* acetone was added to the suspension which was then filtered on silica gel. The clear filtrate was put in a rotary evaporator. After evaporation of the solvent, the solid product was recrystallized from 200 *ml* of 50% aqueous acetone. A yield of 17.76 *g* (69.76%) of white powder was obtained. The structure of the compound was verified by nuclear magnetic resonance spectroscopy and LC-MS spectroscopy.

The preparation of a block copolymer containing a hydrophilic cellophil polymer and a lipid-like copolymer was done by raft polymerization as follows (18):

Preparation 1–2: Step A

In a 50 *ml* round-bottom flask, a solution of 2-(dodecylthiocarbonothioylthio)-2-methylpropionic acid (6.13 *mg*, 0.017 *mmol*), *N*,*N*-Dimethyl acrylamide (0.624 *ml*, 6.05 *mmol*), and *iso*-decyl acrylate (0.163 *ml*, 0.673 *mmol*) in 10 *ml* *N*,*N*-dimethylformamide was degassed using ultrasonic treatment. Subsequently, 2-benzyl-2-(dimethylamino)-4'-morpholinobutyrophenone (6.40 *mg*, 0.017 *mmol*) was added, and polymerization was induced by UV light. After 4 *h* of polymerization under stirring, the reaction mixture was purified by extensive dialysis against deionized water using a membrane with a 3.5 *kDa* MWCO. The mixture was subsequently lyophilized. The average molecular weight (12 *kDa*) and PDI (1.19) of the block copolymer was verified by GPC measurement.

Step B

The lyophilized macro-CTA prepared in step A (300 *mg*, 6.82 μ*mol*) was mixed with acryloyl-*L*-lysine (100 *mg*, 0.499 *mmol*) in 10 *ml* deionized water. The mixture was degassed using ultrasonic treatment. 2,2'-Azobis(2-methylpropionamidine) dihydrochloride (4.62 *mg*, 0.017 *mmol*) was added to the mixture. The polymerization was induced by heating the mixture in a reaction vessel to 50°C. After 4 *h* of polymerization at 50°C, the resulting block copolymer was purified by extensive dialysis against deionized water using a membrane with a 3.5 *kDa* MWCO. The cellophil block copolymer was subsequently lyophilized. The average molecular weight (18 *kDa*) and PDI (1.25) of the block copolymer were verified by GPC measurement. Larger block copolymers (32 *kDa*, PDI 1.28; 58 *kDa*, PDI 1.24) were obtained by decreasing the ratio of CTA to monomers in step A from 1/100 to 1/200 (32 *kDa*) and 1/400 (58 *kDa*), respectively, whereas the molar ratios of *i*-decylacrylate (7.5 *mol* of 5), DMA (63.9 *mol* of 5) and AK (28.6 *mol* of 5) were kept constant.

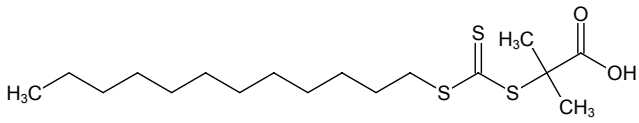
Some of the compounds mentioned in Preparation 1–2 are shown in Figure 1.2.

1.3.2 Silicone Acrylamides

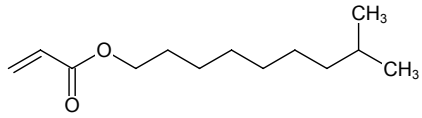
Examples of hydrophilic methacrylamide monomers are collected in Table 1.5. Some of these compounds are shown in Figure 1.3. Also, several other similar monomers have been detailed (22).

These alkyl and aryl groups can be straight or branched. Of these monomers, the *N*-(2-hydroxyethyl)methacrylamide monomer is preferable from a perspective of increasing the transparency of the so obtained polymer.

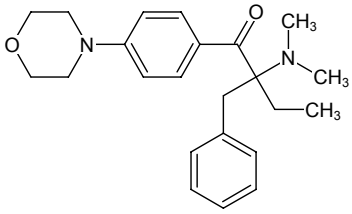
The monomer mixture for synthesizing the polymer additionally may contain between about 1% and about 30% of a hydrophilic



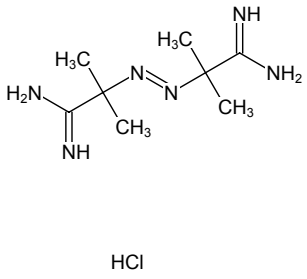
2-(Dodecylthiocarbonothioylthio)-2-methylpropionic acid



iso-Decyl acrylate

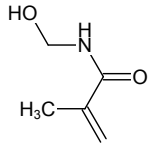


2-Benzyl-2-(dimethylamino)-
4′-morpholinobutyrophenone

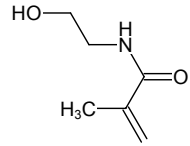


2,2′-Azobis(2-methylpropion-
amidine) dihydrochloride

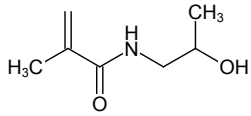
Figure 1.2 Compounds for a block copolymer.



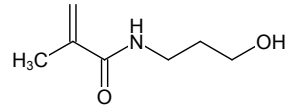
N-Hydroxymethyl methacrylamide



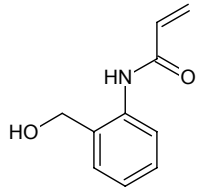
N-(2-Hydroxyethyl) methacrylamide



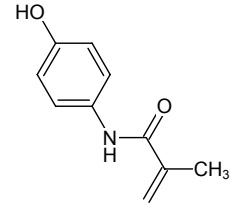
N-(2-Hydroxypropyl) methacrylamide



N-(3-Hydroxypropyl) methacrylamide



N-(2-Hydroxymethylphenyl) methacrylamide



N-(4-Hydroxymethylphenyl) methacrylamide

Figure 1.3 Hydrophilic methacrylamide-based monomers.

Table 1.5 Hydrophilic methacrylamide-based monomers (23).

Compound
N-Hydroxymethyl methacrylamide
N-(2-Hydroxyethyl) methacrylamide
N-(2-Hydroxypropyl) methacrylamide
N-(3-Hydroxypropyl) methacrylamide
N-(2-Hydroxybutyl) methacrylamide
N-(3-Hydroxybutyl) methacrylamide
N-(4-Hydroxybutyl) methacrylamide
N-(2-Hydroxymethylphenyl) methacrylamide
N-(3-Hydroxymethylphenyl) methacrylamide
N-(4-Hydroxymethylphenyl) methacrylamide

polymer with a molecular weight of about 1000 *Dalton* or higher in the monomer and polymer component of the monomer mixture in order to enhance the wettability, resistance to adhesion of proteins, resistance to adhesion of lipids and combinations thereof.

Examples of hydrophilic polymers that can be used in the polymer are shown in Table 1.6. Some of the monomers of these compounds are shown in Figure 1.4.

Hydrophilic polymers selected from poly(vinyl pyrrolidone), poly(*N*,*N*-dimethyl acrylamide), poly(acrylic acid), and poly(vinyl alcohol) may be particularly effective for enhancing the wettability of silicone hydrogels (23). Poly(vinyl pyrrolidone) and poly(*N*,*N*-dimethyl acrylamide) provide a balance between the wettability and the compatibility of the polymerization mix in certain formulations.

The polymer can also include a monomer with two or more reactive groups as a copolymerization component. In this case, the polymer becomes solvent resistent.

Preferable monomers with two or more vinyl groups include bifunctional and polyfunctional acrylates. Examples are shown in Table 1.7. Some bisacrylamide monomers are shown in Figure 1.5. Polyfunctional methacrylate compounds are shown in Figure 1.6.

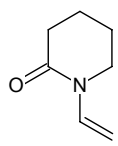
A polymerization initiator may be added to enhance the polymerization traction. Suitable initiators include thermal polymerization initiators, such as a peroxide compound or an azo compound, or

Table 1.6 Hydrophilic polymers (23).

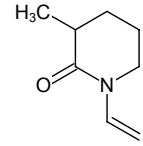
Polymer compound
Poly(*N*-vinyl pyrrolidone)
Poly(*N*-vinyl-2-piperidone)
Poly(*N*-vinyl-2-caprolactam)
Poly(*N*-vinyl-3-methyl-2-caprolactam)
Poly(*N*-vinyl-3-methyl-2-piperidone)
Poly(*N*-vinyl-4-methyl-2-piperidone)
Poly(*N*-vinyl-4-methyl-2-caprolactam)
Poly(*N*-vinyl-3-ethyl-2-pyrrolidone)
Poly(*N*-vinyl-4,5-dimethyl-2-pyrrolidone)
Poly(2-vinylimidazole)
Poly(*N*-vinyl formamide)
Poly(*N*-vinyl acetamide)
Poly(*N*-methyl-*N*-vinyl acetamide)
Poly(*N*,*N*-dimethyl acrylamide)
Poly(*N*,*N*-diethyl acrylamide)
Poly(*N*-isopropyl acrylamide)
Poly(vinyl alcohol)
Poly(acrylate)
Poly(ethylene oxide)
Poly(2-ethyl oxazoline)
Heparine Polysaccharide
Poly(acryloyl morpholine)

Table 1.7 Multifunctional monomers (23).

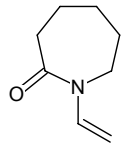
Compound	Compound
Ethylene glycol acrylate	Ethylene glycol dimethacrylate
Diethylene glycol diacrylate	Diethylene glycol dimethacrylate
Triethylene glycol diacrylate	Triethylene glycol dimethacrylate
Neopentyl glycol diacrylate	Neopentyl glycol dimethacrylate
Tetraethylene glycol diacrylate	Tetraethylene glycol dimethacrylate
Glyceryl triacrylate	Glyceryl trimethacrylate
Pentaerythritol tetraacrylate	Pentaerythritol tetramethacrylate
Trimethylol propane triacrylate	Trimethylol propane trimethacrylate
N,*N*′-Methylene bisacrylamide	*N*,*N*′-Ethylene bisacrylamide
N,*N*′-Propylene bisacrylamide	



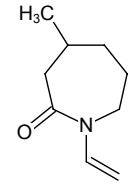
N-Vinyl-2-piperidone



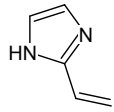
N-Vinyl-3-methyl-2-piperidone



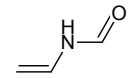
N-Vinyl-2-caprolactam



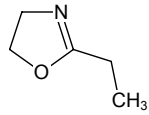
N-Vinyl-4-methyl-2-caprolactam



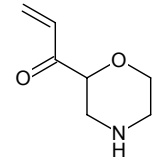
2-Vinylimidazole



N-Vinyl formamide

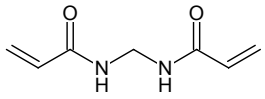


2-Ethyl oxazoline

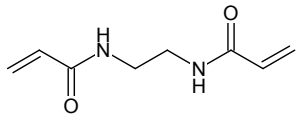


Acryloyl morpholine

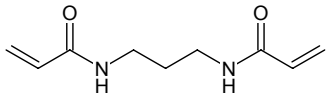
Figure 1.4 Monomers for hydrophilic polymers.



N,*N*′-Methylene bisacrylamide



N,*N*′-Ethylene bisacrylamide



N,*N*′-Propylene bisacrylamide

Figure 1.5 Bisacrylamide monomers.

photopolymerization initiators. Also, photoinitiators can be added in order to enhance the polymerization.

Several examples of the polymerization procedure have been detailed (23).

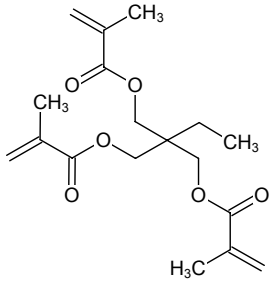
1.4 Soft Lenses

1.4.1 Hydrogels

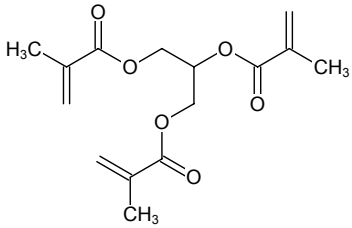
Soft contact lens materials are made by polymerizing and crosslinking hydrophilic monomers such as 2-hydroxyethyl methyacrylate, *N*-vinyl-2-pyrrolidone, and combinations thereof (19).

The polymers produced by polymerizing these hydrophilic monomers exhibit significant hydrophilic character themselves, and are capable of absorbing a significant amount of water in their polymeric matrices. Due to their ability to absorb water, these polymers are often referred to as *hydrogels*.

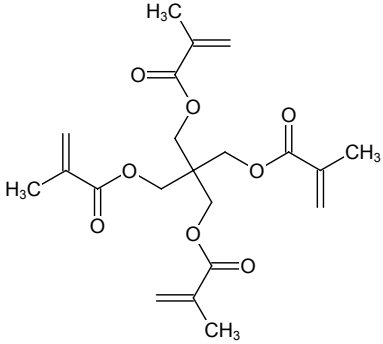
These hydrogels are optically clear and, due to their high levels of water of hydration, are particularly useful materials for making soft contact lenses. However, the high levels of water of hydration of hydrogels contributes to their relative lack of physical strength, which results in hydrogel contact lenses being relatively easy to tear (19).



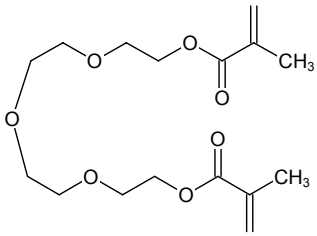
Trimethylol propane trimethacrylate



Glyceryl trimethacrylate



Pentaerythritol tetramethacrylate



Tetraethylene glycol dimethacrylate

Figure 1.6 Polyfunctional methacrylate compounds.