57 CARBOPOL – AN OVERVIEW OF THE MULTIFACETED POLYMER

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ABSTRACT

Carbopol, a synthetic polymer recognized as a multifaceted excipient for its intriguing properties and their extensive applications in pharmaceutical, cosmetics and other industries. It is high molecular weight, hydrophilic, non-toxic and non-irritating powder which is soluble in water, forming a clear, viscous solution which is greatly utilized in formulations, such as creams, ointments, balms and other drug delivery systems. It is a highly pH sensitive polymer and it gets ionized at a range of pH 5.0–9.0, to form viscous gel. This pH dependent responsiveness is utilized in several topical gels, ophthalmic solutions, and oral suspensions. It possesses several revolutionizing features including its capability to modify rheology and providing high viscosity at low concentration makes them a valuable candidate for advanced drug delivery systems.

GENERAL DESCRIPTION

Carbopol, is a synthetic polymer composed of crosslinked network of poly (acrylic acid). It is high molecular weight polymer and hydrophilic, non-toxic, non-irritating, white or off white powder which is soluble in water, forming a clear, viscous solution[1]. It is markedly recognized for its suspending, thickening, gelling, and stabilizing properties. This polymer is greatly utilized in formulations, such as creams, ointments, balms and other drug delivery systems, also in topical applications like lotions, shampoos, and gels. It has wide applications in many household and industrial products, including detergents, air fresheners, and coatings[2][3]. It is very much compatible with various active ingredients. Carbopol 940 is an extremely efficient rheology modifier, capable of providing high viscosity at low concentrations. Hence, Carbopol 940 could be a essential excipient in the formulation of a wide range of products, providing desirable rheological properties, stability, and ease of application[4].

DISCOVERY AND FURTHER HISTORY

Carbomer was first commercialized in 1958 by B.F. Goodrich Company, which is a part of Lubrizol Corporation and soon it was named with a tradename Carbople. It was a breakthrough innovation in polymer chemistry. It is a crosslinked polymer of acrylic acid, recognized for its thickening, stabilizing, and gelling properties. This innovation came out from the efforts to create high-molecular-weight polymers with good rheological behaviors, hoping that it could be best utilized by industries such as pharmaceuticals, cosmetics, and others. Its ability to form transparent, stable gels and emulsions rapidly makes it a multifaceted ingredient in products such as topical medications to cosmetics[5].

Years later, various grades of Carbopol polymer have been developed. These grades differ in properties such as Molecular weight, crosslinked density, and dispersibility. The polymer's adaptability also made it a preferred excipient for controlled-release drug formulations and cosmetic products like lotions and gels. Carbopol is going to play an important role in future on the advancement of drug delivery, especially mucoadhesive and controlled-release drugs. Furthermore, Carbopol's rheological characteristics make it a perfect fit for cutting edge uses like nanotechnology and 3D bioprinting. Its incorporation into sophisticated industrial applications, such as paints and detergents, is also expected to increase. Because of its adaptability, carbopol will remain relevant in a variety of industries, bolstered by continuous scientific and technological developments[5][6].

SYNONYMS

Synonyms for carbopol includes,

- Carbomer
- Polyacrylic acid
- Carboxypolymethylene

TYPES

Carbopol comes in different forms, including interpolymer, co-polymer, and homopolymer. Acrylic acid polymers that have been crosslinked with divinyl glycol or a polyalkenyl polyether are known as carbopol homopolymers. Carbopol 934, which is frequently utilized in medicinal gels and solutions, is one example. High viscosity carbopol 940 is appropriate for transparent gels in personal hygiene products. Carbopol 980, which is comparable to Carbopol 940 but has better consistency and clarity[7]. Copolymers comprising acrylic acid and other monomers, including allyl pentaerythritol, are known as carbopol copolymers. One example is Carbopol 1342, is used in creams and lotions and other applications requiring a stable emulsion. Carbopol 1382 is made for formulations that contain difficult-to-react components, like electrolytes. Carbopol interpolymers are polymers that contain hydrophobic comonomers and acrylic acid. They are made especially for certain uses, such creating water-resistant coatings or providing sensory advantages. One example is Carbopol Ultrez 10, which is utilized in clear formulations and is self-wetting and easily dispersed. Carbopol Ultrez 20 works well in products that contain active components like salts and provides electrolyte tolerance. For compositions needing superior clarity and suspension qualities, Carbopol Ultrez 21 offers exceptional performance.[8] Carbopol® and Noveon® are high-molecular-weight, crosslinked polymers based on acrylic acid. The acrylic acid used in Carbopol® homopolymers is crosslinked with either allyl pentaerythritol or allyl sucrose. Additionally, there are Carbopol® copolymers (containing C10–C30 alkyl acrylate) and interpolymers (containing a long chain alkyl acid ester and a block copolymer of polyethylene glycol). Noveon® polycarbophil is an acrylic acid polymer that has been crosslinked with divinyl glycol.[7][8][9]

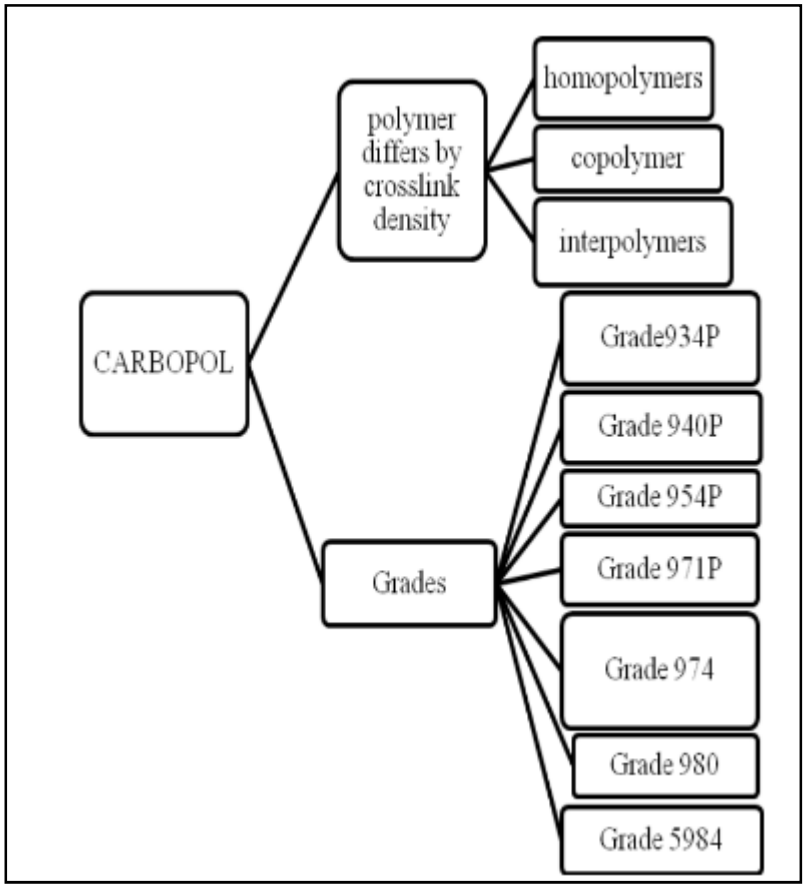

Fig. 57.1 Classification of carbopol

PHYSICOCHEMICAL PROPERTIES

Carbopol is a crosslinked polyacrylic acid polymer, which appears as a white, fluffy, and odorless powder that is highly hygroscopic. It is insoluble in water and non-polar solvents, Rather, these polymers swell when dispersed in water forming a colloidal, mucilage-like dispersion. Carbopol is highly pH-sensitive and they swell in water up to 1000 times their original volume to form a gel when exposed to a pH environment above 4.0 to 6.0. This swelling capability, combined with its ability to retain water up to 1000 times, makes it a good thickening and gelling agent.

Carbopol is generally stable at normal thermal condition but may undergo degradation at high temperatures. It is compatible with a wide range of active ingredients, including drugs, essential oils, and hydrophilic agents, although its stability can be compromised in highly ionic environments due to reduced viscosity[5][10].

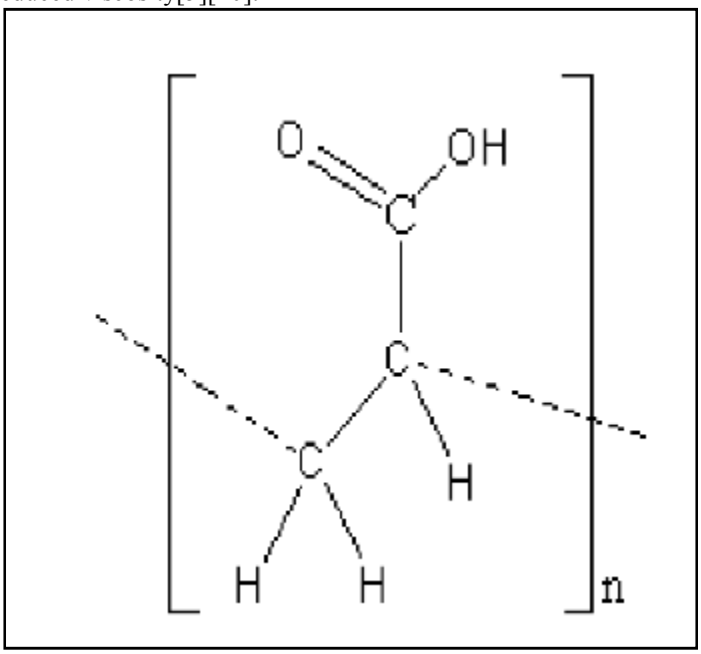

Fig. 57.2 Structure of carbopol polymer

Table 57.1 Physical and Chemical Properties of Carbopol polymer

Appearance	Fluffy, white, mildly acidic polymer
Chemical name	Polyacrylic acid
IUPAC name	Poly(1-carboxyethylene)
Solubility	Insoluble in water and polar solvents
Melting point	116˚c
Molecular weight	72.06 (g/mol)
Molecular formula	(c3h4o2)n
Taste	Bitter
Density	1.2 g/ml at 25˚c
Specific gravity	1.41

METHODS OF SYNTHESIS

Carbopol polymers were first proposed in 1955 and patented in 1957. These polymers are composed of a high molecular weight, crosslinked acrylic acid polymer. Materials are categorized into various categories based mostly on the molecular weight of the polymer chains. Polyacrylic acid is typically produced by free radical polymerization, but graft polymerization can also be employed. Free radical polymerization is the conversion of monomers, in this example acrylic acid (CH_2=$CHCO_2H$), into polymer chains using free radicals. The process normally follows these phases.[11]

1. Initiation: initiators such as potassium persulfate ($K_2S_2O_8$) and azobisisobutyronitrile (AIBN) generate free radicals. These radicals are very reactive and can start the polymerization process by interacting with the monomer molecules.
2. Propagation: when a radical reacts with a monomer, it forms a new radical at the end of the extending chain. This new radical can react with more monomer units, allowing the chain to grow.
3. Termination: The reaction continues until two radicals recombine or a radical is transferred to another molecule, which terminates the polymer chain's growth.
4. Chain transfer and inhibition: Other reactions may occur, such as chain transfer (where the radical is transferred to another molecule, resulting in the formation of a new radical) or inhibition (where impurities hamper the chain's growth)

The carbomer preparation method by using glucose acrylate or glyceryl acrylate:

The invention relates to producing a carbomer from a mixture of acrylic monomers, initiator, crosslinking agent, auxiliary agent, purified water, molten agent, and activated carbon. The solvent consists of tert-butyl alcohol and sorbierite at a molar ratio of 0.3 to 0.7. The initiator is made up of di-t-butyl peroxides, peroxidized t-butyl perbenzoates, and peroxidating trimethylacetic acid tertiary butyl ester. The crosslinking agent is composed of allyl sucroses, glyceryl acrylate, and polypropylene glycol glycidol ether. Tert-butyl alcohol, sorbierite, activated carbon, and filtered water are mixed in a reactor to make the product. The alkalization microwave kettle is then heated to a temperature of 90-70 degrees Celsius before cooling to 65 degrees Celsius utilizing the heat transfer effect. The finished product is then freeze-dried to create a solid carbomer.[12]

FUNCTIONS/USES

Carbopol have a wide range of applications in the pharmaceutical and cosmetic field due to their high viscosity at low concentration, wide viscosity interval and characteristic flow behavior, compatibility with many active ingredients, good thermal stability, excellent organoleptic characteristics, good patient acceptance and a potential candidate for use in controlled release drug delivery system. Carbopol polymers are used in a diverse range of pharmaceutical applications to provide controlled release in tablets, Bioadhesion in buccal, ophthalmic, intestinal, nasal, vaginal and rectal applications.

DRUG DELIVERY SYSTEM

Controlled Drug Delivery System

Carbopol, are high molecular weight polymer widely used in pharmaceutical formulations for their gel-forming capabilities. Upon hydration, they swell to form hydrogels, making them suitable as hydrogel framework materials in controlled-release preparations. In sustained-release formulations, carbopols are effective at low concentrations, typically ranging from 5% to 10% of the total formulation, depending on the drug properties and desired release profile. This efficiency allows for smaller tablet sizes and offers flexibility in prescription design. Additionally, carbopol exhibit excellent compressibility and compatibility with other excipients[13].

Bioadhesive Drug Delivery System

Carbopol (carbomer 934) is useful in several therapeutic applications due to its potent bioadhesive properties. In vivo investigations using gamma scintigraphy shows carbomer 934, when compared to non-adhesive materials like ethylcellulose, greatly decreases the migration rate of granules in the alimentary canal, suggesting a stronger interaction with the gastrointestinal mucus layer. By lengthening the duration of a drug's occupancy at the site of absorption, this bioadhesive property improves bioavailability. Because prolonged mucosal adherence is advantageous, carbomer 934 is used in formulations including nasal and oral bioadhesive preparations [14].

Ophthalmic Formulations

Viscous eye drops based on carbomer are used to treat dry eye syndrome which offers longer-lasting lubrication than polyvinyl alcohol (PVA) based artificial tears. carbomer, due to their high viscosity, gels have a longer corneal contact time, which prolongs the time it takes for the tear film to break up and reduces the frequency of application. In comparison to PVA eye drops, carbomer drops relieves symptoms like dryness which is demonstrated by several clinical studies. Though more research is required to maximize the advantages of carbomer eye drops and resolve any tolerability issues, the results indicate that they are a viable alternative for treating dry eyes. [15].

Topical Drug Delivery System

Carbopol polymers, a multifaceted excipient, have shown great potential in topical drug delivery systems. These polymers offer unique physicochemical properties such as gel-forming capabilities, viscoelastic behavior, and thermal stability, making them highly adaptable to various APIs and innovative formulations. Their compatibility and performance characteristics have made Carbopol polymers a valuable tool in overcoming traditional limitations of topical delivery[16].

Oral Suspension

Carbopol polymers have been widely used in oral suspensions to thicken, modify flow properties, suspend insoluble ingredients and provide bioadhesion. The significance of these polymers is that they eliminate the settling problem even at low concentrations. As carbopol polymers swell when hydrated and neutralized, they form colloidal dispersion. They are highly efficient at low level and provide long term stability of suspension over wide pH range. Also they can be used to build viscosity and to mask the bitter taste of certain drugs[5][17].

HANDLING PRECAUTION

The quality and safety of carbopol is maintained by proper storage and handling. It should be handled carefully in order to prevent the formation of aerosols since it has the risk of igniting due to electrostatic discharge. Non- sparking tools should be used for safe handling. Additionally, personal protective equipment, such as tightly fitting safety goggles, flame-resistant and impervious clothing, and gloves, should always be used to ensure safety during handling. Adhering to these guidelines ensures the efficacy and safety of carbopol during its storage and use. [17][18].

STORAGE

Carbopol is chemically stable when stored in normal storage conditions and has a two year shelf life period. . Studies suggest that these polymers can remain stable for at least five years in their dry powder form, with no significant changes in chemical parameters or detected impurities during this period. Carbopol can absorb moisture from the environment as it is hygroscopic in nature. Even though they are shipped with a maximum moisture content of 2%, they can reach 8% equilibrium moisture when exposed to open air at room temperature and 50% relative humidity. Though moisture absorption does not affect their efficiency, it makes the polymers harder to weigh and disperse accurately. Hence 8it is essential to store these polymers in tightly sealed containers and away from water.

The efficacy of the carbopole is not affected by the heat exposure below 104°C (220°F) for up to two hours, but extreme heat can cause sintering, which alters the drug release properties. It makes the polymer harder to handle, and may lead to discoloration or decomposition. At elevated temperatures like 260°C (500°F), it undergoes complete degradation within 30 minutes. It is suggested to store carbopol polymers in a cool, dry environment to maintain their quality. Regular re-testing for moisture content, humidity levels is required once every 6–12 months. These precautions ensure that polymers remain effective and manageable throughout their storage life[19].

INCOMPATIBILITIES

Carbopol, despite its applications, has incompatibilities with certain substances. It is sensitive to electrolytes, as the presence of salts can reduce its viscosity and thickening ability due to charge screening effects. Additionally, carbopol may not perform well in formulations containing cationic surfactants or compounds because these can neutralize its anionic nature, leading to precipitation or loss of gel structure. Certain organic solvents, like alcohols in high concentrations, may also affect its gelling properties by reducing hydration. Carbopol is pH- sensitive and it has an optimal performance occurring in the range of pH 5 to 9. It undergoes degradation (or) unstable at extreme acidic or alkaline conditions. Proper formulation design is essential to mitigate these incompatibilities and ensure desired product performance [20][21].

ADVERSE EFFECTS

Carbopol possesses certain adverse effects especially eye irritation. Accidental introduction of dry powder and dispersion with a pH of 3 or below 3, into the eyes can cause minor irritation. Carbopol forms a gelatinous film on hydration which can increase the difficulty of removal and potential eye damage. Carbopol Application on skin, generally causes a mild irritation, with slight redness and swelling. dermatitis or sensitization is also observed on repeated or extended use. Carbopol ingestion in large quantities during animal studies shows gastrointestinal irritation, though no pathological changes were observed. Despite these effects, carbopol is considered safe for use in pharmaceutical and cosmetic formulations when used as per recommended guidelines[21].

EVALUATION

Viscosity

Carbopole's viscosity ranges between 29400 and 39400 centipoises and it is determined by the following method:

Fix a stirrer capable of running at a speed of 1000 ± 10 rpm in a 1000-liter beaker containing 500 ml of water. Position the shaft at an angle of 60° to one side of the beaker and the propeller toward the bottom. Add 2.5 g of powder gradually and evenly throughout 45-90 seconds, breaking up any loose aggregates. Stir continuously at 1000±10 rpm for 15 minutes. Remove the stirrer and immerse the beaker and its contents in a water bath at 25°

± 0.2° for 30 minutes. Insert the stirrer to a depth necessary to ensure that air is not drawn into the dispersion and continue stirring at 300±10 rpm. Titrate with a calomel-glass electrode system to a pH of 7.5±0.3 by adding an 18% w/v solution of sodium hydroxide below the surface, the end-point being determined potentiometrically (approximately 6.2 ml of the sodium hydroxide solution will be

required). Allow 2 to 3 minutes before final determination of pH. If the final pH exceeds 7.8, discard the mucilage and predetermine the pH by using a lesser quantity of the sodium hydroxide solution for titration. Place this mucilage in the water bath at 25℃ for 1 hour, and determine its viscosity by Method C, Appendix 8.14, without delay to avoid slight viscosity changes possible after 75 minutes of alkali addition. To operate a spinning viscometer, use a spindle with a 1.47 cm diameter and 0.16 cm height coupled to a 0.32 cm diameter shaft. The distance from the cylinder to the lower tip of the shaft should be 3.02 cm, and the immersion depth should be 4.92 cm (No. 6 spindle). Rotate the spindle at 20 rpm and record the scale reading on the viscometer. Calculate the viscosity in centipoises by multiplying the scale reading with the spindle constant at 20 rpm[22].

Acidity

1% w/v dispersion yields orange color with thymol blue solution and yellow color with cresol red solution (pH around 3) [23].

MARKETED PRODUCTS

Table 57.2 Marketed Products Of Carbopol Polymer [23] [24] [25]

Brand Name	Company name	Unit	Price (INR)
Carbopol 980 Powder	OLL Chem Inc	25kg	10,500/-
Carbopol 934 P/ 971 P/ 974 P	Yarrowpharm	500g 1kg	2,975/- 4,975/-
ol 940 (Carboxy Vinyl Polymer 940)	Yarrowpharm	250g 500g 1kg	1750/- 2975/- 3975/-
Carbopol 980 Powder	Oryn Healthcare LLP	20kg	11,300/-
Lubrizol Carbopol 940 Powder	Mahima Biotech Private limited	50kg	23,000/-

PATENTS

Table 57.3 Patents Of Carbopol Polymer

S.NO	Invention name	Inventor name	Date of grant	Application number
1.	Carboxylic polymers	Harold P. Brown, Akron, Ohio.	July 2nd, 1957	US 2, 798, 053
2.	Ophthalmic compositions containing a synergistic combination of two polymers.	asood A. Chowhan & Huagang Chen	May 24, 2011	US 7, 947, 295, B2
3.	A kind of Carbomer and preparation method by using vinylformic acid sucrose ether or pentaerythritrol triallyl ether.	Zhang Li, Hu Wanrong, Chen Yue, Zhou Jungang, Peng Danyuanjing, Wu Lingli, Luo Rongzhen	January 1st, 2014	201310453464.3
4.	A kind of carbomer and preparation method by using glucose acrylate or glyceryl acrylate	Zhang Li, Hu Wanrong, Chen Yue, Zhou Jungang, Peng Danyuanjing, Wu Lingli, Luo Rongzhen	April 30th, 2014	201410010540.8

CONCLUSION

Carbopol, an useful excipient has a wide range of applications in pharmaceutical, cosmetics, industrial fields due to its intriguing properties like suspending, thickening, gelling, and stabilizing properties. It also exhibits exceptional properties like rheology modifying, high viscosity even at low concentrations, and its ability to form transparent, stable gels, emulsions. When the polymer combined with strong bioadhesive properties makes them a potentially valuable excipient in modern drug delivery systems including mucoadhesive and controlled-release systems. Moreover its pH-sensitive swelling behavior allows for controlling viscosity and gel formation precisely. It can be utilized in developing innovative drug delivery systems as they possess additional qualities including thermal stability, excellent compressibility and their compatibility with extensive active ingredients. In comparison to conventional polymers, carbopol is an excellent and indispensable polymer in both traditional and modern drug development.

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