INTRODUCTION

Gels are semirigid systems in which the movement of the dispersing medium is restricted by an interlacing three-dimensional network of particles or solvated macromolecules of the dispersed phase. A high degree of physical or chemical cross-linking may be involved. The increased viscosity caused by the interlacing and consequential internal friction is responsible for the semisolid state. A gel may consist of twisted, matted strands often wound together by stronger types of van der Waals forces to form crystalline and amorphous regions throughout the system, e.g. tragacanth and carboxymethylcellulose.

Some gel systems are as clear as water in appearance and others are turbid, since the ingredients may not be completely molecularly dispersed or they may form aggregates, which disperse light. The concentration of the gelling agents is mostly less than 10%, usually in 0.5 to 2.0% range.

According to the USP, gels or jellies are semisolid systems consisting of suspensions made up of small inorganic particles or of large organic molecules interpenetrated by a liquid. Where the gel mass consists of a network of small discrete particles, the gel is classified as a two-phase system. In these two-phase systems, if the particle size of the dispersed phase is large, the product is referred to as a magma. Single-phase gels consist of organic macromolecules uniformly distributed throughout a liquid in such manner that no apparent boundaries exist between the dispersed macromolecules and the liquid. Single-phase gels may be made from synthetic macromolecules or from natural gums (mucilages). The continuous phase usually is aqueous but it also can be alcoholic or oleaginous.

For best consumer appeal, gels should have clarity and sparkle. Most gels are water washable, water soluble, water absorbing, greaseless, and act as absorption bases. The gel should also maintain its viscosity and character over a wide temperature range.

TERMINOLOGY RELATED TO GELS

Imbibition is the taking up of a certain amount of liquid without measurable increase in volume.

Swelling is the taking up of a liquid by a gel with an increase in volume. Only those liquids that solvate a gel can cause swelling. The swelling of protein gels is influenced by pH and the presence of electrolytes.

Syneresis occurs when the interaction between particles of the dispersed phase becomes so great that on standing, the dispersing medium is squeezed out in droplets and the gel shrinks. Syneresis is a form of instability in aqueous and nonaqueous gels. Separation of a solvent phase is thought to occur because of the elastic contraction of the polymeric molecules: in the swelling process during gel formation the macromolecules involved become stretched and the elastic forces increase as swelling proceeds. At equilibrium, the restoring force of the macromolecules is balanced by the swelling forces, determined by the osmotic pressure. If the osmotic pressure decreases, e.g. on cooling, water may be squeezed out of the gel. The syneresis of an acidic gel from Plantago albiacar seed gum may be decreased by the addition of electrolyte, glucose and sucrose, and by increasing the gum concentration. pH has a marked effect on the separation of water. At low pH marked syneresis occurs in carboxypolymethylene gels, possibly due to suppression of ionization of the carboxylic acid groups, loss of hydrating water, and the formation of intramolecular hydrogen bonds. This would reduce the attraction of the solvent for the macromolecule.

Thixotropy is a reversible gel-sol formation with no change in volume or temperature—a type of non-Newtonian flow.

A xerogel is formed when the liquid is removed from a gel and only the framework remains. Examples would include gelatin sheets, tragacanth ribbons and acacia tears.

APPLICATION OF GELS

Gels have a variety of applications in the administration of medications orally, topically, intranasally, vaginally and rectally. Gels can serve as ointment bases. Examples are Plastibase™ and mineral oil gels made with aluminum monostearate.

Nasal absorption of drugs from gels has been investigated extensively. Some reports of drugs administered by nasal methylcellulose gels, e.g. propranolol, show the drug is better absorbed than when administered orally.

CLASSIFICATIONS AND TYPES OF GELS

Table 1 is a general classification of gels, listing two classification schemes. The first scheme divides gels into “inorganic” and “organic”.
Inorganic Hydrogels are usually two-phase systems such as Aluminum Hydroxide Gel and Bentonite Magma. Bentonite also has been used as an ointment base in about 10-25% concentrations.

Organic Gels are usually single-phase systems and may include such gelling agents as carbomer and tragacanth and those that contain an organic liquid, such as Plastibase™.

The second classification scheme divides gels into hydrogels and organogels with some additional subcategories.

Hydrogels include ingredients that are dispersible as colloids or are soluble in water and include organic hydrogels, natural and synthetic gums, and inorganic hydrogels. Examples are hydrophilic colloids such as silica, bentonite, tragacanth, pectin, sodium alginate, methylcellulose, sodium carboxymethylcellulose and alumina, which in high concentration, form semisolid gels. Sodium alginate has been used to produce gels that can be employed as ointment bases. In concentrations greater than 2.5% and in the presence of soluble calcium salts, a firm gel, stable between pH 5 and 10, is formed. Methylcellulose, hydroxyethylcellulose and sodium carboxymethylcellulose are among the commercially available cellulose products that may be used in ointments. They are available in various viscosity types, usually high, medium and low.

Organogels include the hydrocarbons, animal/vegetable fats, soap base greases and the hydrophobic organogels. Included in the hydrocarbon type is Jelene, or Plastibase, a combination of mineral oils and heavy hydrocarbon waxes with a molecular weight of about 1300. Petrolatum is a semisolid gel consisting of a liquid component together with a "protosubstance" and a crystalline waxy fraction. The crystalline fraction provides rigidity to the structure, while the protosubstance or gel former stabilizes the system and thickens the gel. The hydrophilic organogels, or polar organogels, include the polyethylene glycols of higher molecular weight, the Carbowaxes. They are soluble to about 75% in water and are completely washable. They gels look and feel like petrolatum. They are nonionic and stable.

Jellies are gels in which the structural coherent matrix contains a high proportion of liquid, usually water. They are usually formed by adding a gelling agent such as tragacanth or carboxymethyl cellulose to an aqueous solution of a drug substance. The resultant product is usually clear and of a uniform semisolid consistency. Jellies are subject to bacterial contamination and growth and thus most are preserved with antimicrobials. Jellies should be stored with tight closures since water may evaporate, drying out the product.

Some substances, such as acacia, are termed natural colloids because they are self-dispersing in a medium. Other materials that require special treatment for prompt dispersion are called artificial colloids. The special treatment may involve fine pulverization to colloidal size with a colloidal mill or a micropulverizer.

**GELLING AGENTS**

Examples of gelling agents include acacia, alginic acid, bentonite, carbomer, carboxymethylcellulose sodium, cetostearyl alcohol, colloidal silicon dioxide, ethylcellulose, gelatin, guar gum, hydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium aluminum silicate, maltodextrin, methylcellulose, polyvinyl alcohol, povidone, propylene carbonate, propylene glycol alginate, sodium alginate, sodium starch glycolate, starch, tragacanth and xanthan gum. A few of the more common ones will be discussed here.

**Algic acid** is obtained from seaweed throughout the world and the prepared product is a tasteless, practically odorless, white to yellowish-white, fibrous powder. It is used in concentrations between 1% and 5% as a thickening agent in waters. It swells in water to about 500-2000 times its own weight without dissolving. Crosslinking with increased viscosity occurs upon the addition of calcium salt, such as calcium citrate. Algic acid can be dispersed in water vigorously stirred for approximately 30 minutes. Premixing with another powder or with a water-miscible liquid aids in the dispersion process.

**Bentonite**, a naturally occurring hydrated aluminum silicate, can be used to prepare gels by sprinkling the bentonite on the surface of hot water until the mass is homogeneous. After standing 24 hours, stirring occasionally, the bentonite has become wetted. Glycerin or a similar liquid can be used to pre-wet the bentonite prior to mixing with water. Aqueous bentonite suspensions retain their viscosity above pH 6 but are precipitated by acids. Alkaline materials, such as magnesium oxide, increase gel formation. Alcohol in significant amounts can precipitate bentonite and, since bentonite is anionic, the antimicrobial efficacy of cationic preservatives may be reduced. Bentonite exhibits thixotropy: it may form a semirigid gel which reverts to a sol when agitated. The sol will re-form to a gel upon standing.

**Carbomer** (Carbopol®) resins were first described in the literature in 1955 and are currently ingredients in a variety of pharmaceutical dosage systems, including controlled release tablets, oral suspensions and topical gels. The USP-NF, British Pharmacopoeia, United States Adopted Names Council (USAN) and Cosmetic, Toiletries and Fragrance Association (CTFA) have adopted the generic name “carbomer” for the Carbopel family of resins. Carbomer resins are high molecular weight, allyl-pentaerythritol-crosslinked, acrylic acid-based polymers, modified with C10-C30 alkyl acrylates. They are fluffy, white, dry powders with large bulk densities, 2% maximum moisture, pH5 of 6.0±0.5. The pH of 0.5% and 1.0% aqueous dispersions are 2.7-3.5 and 2.5-3.0, respectively. There are many carbomer resins, with viscosity ranges from 0 to 80,000 cps. The resins commonly used in pharmacy are listed in Table 2.

**Carbomers 910, 934, 934P, 940 and 1342** are official in USP 23/NF 18. Carbomer 910 is effective at very low concentrations when low viscosity is desired and is frequently used for producing stable suspensions. It is the least ion sensitive of these resins. Carbomer 934P is highly effective in thick formulations such as viscous gels. The two alternative resins, numbers 2984 and 5984, are polymerized in ethyl acetate/cyclohexane in place of benzene. Carbomer 934P is similar to 934 but is intended for oral and mucosal contact applications and is the most widely used in the pharmaceutical industry. In addition to thickening, suspending and emulsifying in both oral and topical formulations, the 934 polymer is also used to provide sustained-release properties in both the stomach and intestinal tract for commercial products. Carbomer 941, or 981, its cosolvent alternative, forms sparkling clear aqueous or hydroalcoholic gels. These are the most efficient of all the Carbopol resins and have very good non-drip properties. Carbomer 1342 and its cosolvent analogue, 1382, provide pseudoplastic rheology which is very effective in preparing pourable suspensions and stable emulsions and makes them especially good for preparations containing dissolved salts.

**Carbopol 974P NF** differs from Carbopol 934P NF in that ethylacetaetate is used instead of benzene in its preparation. Carbopols 980 NF and ETOL 2001 differ from Carbopol 940 NF in that cosolvents are used in place of benzene for their preparation. Such is also the case with Carbopols 981 NF and ETOL 2050 vs Carbopol 941 NF.

The addition of alcohol to prepared carbomer gels may decrease their viscosity and clarity. To overcome the loss of viscosity, an increase in the concentration of carbomer may be required; the amount may vary depending upon the pH of the product. When working with a preparation at pH 5.5 and going from 0% to 50% alcohol, an increase of 0.5% carbomer is required; similarly, an increase of 0.35% carbomer is required when going from 20% to 40% alcohol. Above this point, gel viscosity is dependent upon the presence of electrolytes and the pH. Generally, a maximum of 3% electrolytes can be added before a rubbbery mass forms. Overneutralization also will result in decreased viscosity that cannot be reversed by the addition of acid. Maximum
Carbomer preparations can be used to pre-wet the powders. Maximum

<table>
<thead>
<tr>
<th>Product</th>
<th>Viscosity*</th>
<th>Properties and Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbopol 907</td>
<td>0-3,000</td>
<td>Very water soluble. Good lubricity at low viscosity. A &quot;linear&quot; polymer that is not cross-linked.</td>
</tr>
<tr>
<td>Carbopol 910NF</td>
<td>3,000-7,000</td>
<td>Effective in low concentrations. Good ion tolerance.</td>
</tr>
<tr>
<td>Carbopol 934 NF</td>
<td>30,500-39,400</td>
<td>Good stability at high viscosity. Good for thick formulations, such as medium to high viscosity gels, emulsions and suspensions.</td>
</tr>
<tr>
<td>Carbopol 2984</td>
<td>45,000-80,000</td>
<td></td>
</tr>
<tr>
<td>Carbopol 5984</td>
<td>25,000-45,000</td>
<td></td>
</tr>
<tr>
<td>Carbopol 934 NF</td>
<td>29,400-39,400</td>
<td>Good for order-release of products, such as oral and mucosal applications. Excellent for transdermals and topicals.</td>
</tr>
<tr>
<td>Carbopol 974 NF</td>
<td>29,400-39,400</td>
<td></td>
</tr>
<tr>
<td>Carbopol 940 NF</td>
<td>40,000-60,000</td>
<td>Excellent thickening efficiency at high viscosities and very good clarity.</td>
</tr>
<tr>
<td>Carbopol 980 NF</td>
<td>40,000-60,000</td>
<td>Produces sparkling clear aqueous or hydroalcoholic topical gels.</td>
</tr>
<tr>
<td>Carbopol ETD 2001</td>
<td>45,000-65,000</td>
<td></td>
</tr>
<tr>
<td>Carbopol 941 NF</td>
<td>4,000-11,000</td>
<td>Produces low viscosity sparkling clear gels. Good stabilizer for emulsions.</td>
</tr>
<tr>
<td>Carbopol 981 NF</td>
<td>4,000-11,000</td>
<td>Effective in moderate ionic systems. More efficient than 934 and 940 at low to moderate concentrations.</td>
</tr>
<tr>
<td>Carbopol ETD 2050</td>
<td>3,000-15,000</td>
<td></td>
</tr>
</tbody>
</table>

*Typical viscosities of a 0.5% solutions, pH 7.5, except for Carbopol 907 which was a 4.0% solution.

viscosity and clarity occur at pH 7, but acceptable viscosity and clarity begins at pH 4.5 to 5.0 and extends to a pH of 11.

Crosslinked carbomer resins may swell in water up to 1000 times their original volume to form gels, when exposed to a pH environment above 4.0-6.0. Since the pH of these polymers is about 6.0, the carboxylate groups are incompletely ionized, resulting in repulsion between the negative particles of the polymer backbone which contributes to the swelling of the polymer. It is difficult to determine the molecular weight of the carbomers and while the average molecular weights of the polymerized resins are in the order of about 500,000, the actual molecular weight of the crosslinked resin is in the billions.

Carbomer resins are very hygroscopic and should be stored in tight containers, away from moisture and extreme temperatures. Moisture does not affect the efficiency of the resins, but high levels make them more difficult to disperse and weigh accurately. Autoclaving appears to have no effect on the viscosity or pH of the prepared dispersions of a carbomer that have not been neutralized can be stored as stock solutions at concentrations up to 5%.

Carbomer resin powders do not support bacteria, mold or fungus while in powder form. When present in aqueous systems, however, mold and some bacteria can grow. Table 3 lists commonly used preservatives and their compatibility with carbomer resins. The addition of 0.1% methylparaben or propylparaben as preservatives is acceptable and does not affect the resins’ efficiency. Carbomer resins are anionic and may decrease the efficiency of some of the cationic preservative agents.

Glass, plastic or resin-lined containers are recommended for storage of carbomer products. Aluminum tubes should be used only when a product as a pH of less than about 6.5. With other metallic materials, a pH of about 7.7 or greater is preferred. Cleaning up equipment after preparing carbomer products is easier using warm water containing salt, a commercial detergent and an anionic surfactant. Carbomers are very hygroscopic and should be stored in tight containers, away from moisture and extreme temperatures. Carbomer resins are very hygroscopic and should be stored in tight containers, away from moisture and extreme temperatures.

Preparation of aqueous dispersions of carbomer resins: Carbomer preparations are primarily used in aqueous systems, although other liquids can be used. In water, a single particle of carbomer will wet very rapidly but, like many other powders, carbomer polymers tend to form clumps of particles when haphazardly dispersed in cold water. The surfaces of these clumps solvate, a layer is formed which prevents rapid wetting of the interior of the clumps. When this occurs, the slow diffusion of solvent through this solvated layer determines the mixing or hydration time. To achieve fastest dispersion of the carbomer, it is wise to take advantage of the very small particle size of the carbomer powder by adding it very slowly into the vortex of the liquid as it is stirred very rapidly. Almost any device, like a simple sieve, that can sprinkle the powder on the rapidly stirred liquid is useful. A metallic screen will help by reducing the particle size and diffusing static charge buildup. Generally, the higher the agitation rate of the liquid, the better, but extremely high shear rates should not be used as they can break down the polymers and reduce gel viscosity. Propeller or turbine type mixers running about 800-1200 rpm work very well for this purpose. Variable speed mixers are especially desirable to reduce vortexing when the mixture begins to thicken and will help minimize the incorporation of air into the gel. The propeller should be located very close to the bottom of the mixing vessel. The goal is to prevent clumping by slowly sprinkling the very small particle size powder over the rapidly agitated water. Once the powder is incorporated, continued stirring for 10-15 minutes at reduced speed is recommended to avoid excess air entrapment.

A neutralizer is added to thicken the gel after the carbomer is dispersed. Sodium hydroxide or potassium hydroxide can be used in carbomer dispersions containing less than 20% alcohol. Triethanolamine will neutralize carbomer resins containing up to 50% ethanol. Other neutralizer agents include sodium carbonate, ammonia and borax.

Air bubbles incorporated into the gel should be removed prior to adding the neutralizing agent, otherwise the air will remain entrapped in the product. Air bubbles can be removed using an ultrasonic unit or by allowing the product to stand. It may be necessary to acidify the gel, remove the air and neutralize it again. For this, hydrochloric and phosphoric acid should be used in an amount equal to 0.5% based on the weight of the carbomer, NOT the total weight of the product. These acids will not produce significant salt levels upon neutralization that might occur with other acids, e.g. citric or lactic.

Carboxymethylcellulose in concentrations of 4 to 6% of the medium viscosity grades can be used to produce gels; glycerin may be added to prevent drying. Precipitation can occur at pH values less than 2; it is most stable at pH levels between 2 and 10, with maximum stability at pH 7 to 9. It is incompatible with ethyl alcohol.

Carboxymethylcellulose Sodium (CMC Sodium): Sodium carboxymethylcellulose is soluble in water at all temperatures. The sodium salt of CMC can be dispensed with high shear in cold water before the particles can hydrate and swell to sticky gel grains that agglomerate into lumps. Once the powder is well dispersed, the solution is heated with moderate shear to about 60˚C for fastest dissolution. These dispersions are sensitive to pH changes because of the carboxylate group. The viscosity of the product is decreased markedly below pH 5 or above pH 10.

Colloidal silicon dioxide can be used to prepare transparent gels when used with other ingredients of similar refractive index. Colloidal silicon adsorbs large quantities of water without liquefying. The viscosity is largely dependent on temperature. Changes in pH may affect the viscosity; it is most effective at pH values up to about 7.5. At higher levels, the viscosity-increasing properties are reduced at pH greater than 10.7 and the silicon dioxide dissolves to form silicates with no viscosity-increasing properties. Colloidal silicon dioxide (fumed silica) will form gels when combined with 1-dodecanol and n-dodecane. These are prepared by adding the silica to the vehicle, sonating for about one minute to obtain a uniform dispersion, sealing and storing at about 40˚C overnight to complete gelation. This gel is more hydrophobic in nature than the others.

Gelatin: Gels are prepared from gelatin by dispersing the gelatin in hot water followed by cooling. As an alternative, moisten the gelatin with about 3 to 5 parts of an organic liquid that will not swell the polymer, such as ethyl alcohol or propylene glycol, add the hot water and cool.

Magnesium aluminum silicate, Veegum, in concentrations of about 10%, forms firm, thixotropic gels. The material is inert and has few incompatibilities but is best used above pH 3.5. It may bind to some drugs and limit their availability.

Methylcellulose is a long-chain substituted cellulose that can be used to form gels in concentrations up to about 5%. Since methylcellulose hydrates slowly in hot water, the powder is dispersed with high shear in about 1/3 of the required amount of water at 80-90˚C. Once the powder is finely dispersed, the rest of the water is added cold or as ice with moderate stirring to cause prompt dissolution. Anhydrous alcohol or propylene glycol may be used to help pre-wet the powders. Maximum
is used as a gelling agent in concentrations of 1 to 5%, depending upon the specific application. The preparations are most stable at a pH of 3-6 and should contain a preservative.

Sodium alginlate can be used to produce gels in concentrations up to 10%. Aqueous preparations are most stable between pH 4-10; below pH 3, alginic acid is precipitated. Sodium alginlate gels for external use should be preserved with, for example, 0.1% chloroxylenol or the parabens. If the preparation is acidic, benzoic acid may be used. High concentrations will result in increased viscosity up to a point where the sodium alginlate is salted out; it occurs at about 4% with sodium chloride.

Tragacanth gum has been used to prepare gels that are most stable for pH 4-8. These gels must be preserved with either 0.1% benzoic acid or sodium benzoate or a combination of 0.17% methylparaben and 0.03% propylparaben. These gels may be sterilized by autoclaving. Since powdered tragacanth gum tends to form lumps when added to water, aqueous dispersions are prepared by adding the powder to vigorously stirred water. Also, the use of ethanol, glycerin or propylene glycol to pre-wet the tragacanth is very effective. If other powders are to be incorporated into the gel, they can be mixed with the tragacanth in the dry state.

**Example Gel Formulations**

**Starch Glycerite**

- **Starch**: 100 g
- **Benzoic Acid**: 2 g
- **Glycerin**: 700 g
- **Propylene glycol**: 200 g
- **Phosphate Buffer**: 1% of a solution of phosphoric acid may be used. High concentrations will result in increased viscosity up to a point where the starch grains are salted out; it occurs at about 4% with sodium chloride.

**Bentonite Magma**

- **Bentonite**: 50 g
- **Glycerin**: 100 mL

Bentonite is sprinkled on 800 mL of hot purified water and allowed to hydrate for 24 hours, with occasional stirring. Additional Purified Water is added to make 1000 mL. If a mechanical blender is used, approximately one-half of the water is placed in the blender, and the bentonite is added while the blender is in operation. Purified water is then added to make the volume of 1000 mL and the blender is operated for 10 minutes.

**Liquid-solid Emulsion Gel**

- **Gelatin Solution**: Gelatin, 200 bloom
- **Phosphate Buffer**: pH 7
- **Gel Product**: Gelatin Solution
- **Long chain alcohol**: 10 g

Liquid-solid emulsion gels can be prepared from gelatin and a selection of an alcohol from a homologous series, e.g., octanol, nonanol, decanol, undecanol or dodecanol. The initial step involves the formulation of an aqueous gelatin base such as 20% (w/w) 200 bloom gelatin in phosphate buffer (pH 7.0) prepared by melting (at 60°C) the gelatin/water mixture which has previously matured for about one hour at room temperature. The molten gel is left at 60°C for a further two hours to allow escape of air bubbles. Next, 10 g of the long-chain alcohol, preheated to 60°C, is added to 40 g of the heated molten aqueous gel and stirred at high speed for about two minutes. The drug can be previously added to the appropriate phase. The molten mixture is poured onto a plate or between two plates to set or “cast”. Circular or other shaped portions of the gel can be cut out and applied to the skin area to release the enclosed drug.

**Liqua-Gel™ (Paddock)** is a non-greasy, water soluble liquid lubricating gel that can be used to dissolve or suspend a variety of topically-applied dermatological agents. It contains purified water, propylene glycol, glycerin, hydroxypropyl methylcellulose, and potassium sorbate. Sodium phosphate and borax acid are used to buffer the gel to a pH of about 5.0. Diazolidinyl urea, methylparaben and propylparaben are included as preservatives. It is a clear, colorless gel with a faint characteristic odor which is very viscous at 25°C.

**Lubricating Jelly Formula**:  
- **Methylcellulose, 4000 cps**: 0.8%  
- **Carbopol 934**: 0.24%  
- **Propylene glycol**: 16.7%  
- **Methylparaben**: 0.015%  
- **Sodium hydroxide, qs ad**: pH 7

Report the pH of the dispersion to 7.0 by adding sufficient 1% sodium hydroxide solution (about 12
When swallowing a tablet is a problem...

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- Allopurinol
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- Cisapride
- Clonazepam
- Diltiazem HCl
- Dipyridamole
- Enalapril Maleate
- Flecainide Acetate
- Flucytosine
- Hydralazine HCl
- Ketoconazole
- Labetalol
- Metolazone
- Metoprolol Tartrate
- Metronidazole
- Procainamide
- Pyrazinamide
- Quinidine Sulfate
- Rifampin
- Spironolactone
- Spironolactone/HCTZ
- Tetracycline HCl
- Verapamil HCl
mL is required) and bring the volume to 40 mL with purified water. Dissolve the methylparaben in the propylene glycol. Mix the methylcellulose, Carbopol 934 and propylene glycol fractions, using caution to avoid incorporating air.

Clear Aqueous Gel with Dimethicone

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>59.8%</td>
</tr>
<tr>
<td>Carbomer 934</td>
<td>0.5%</td>
</tr>
<tr>
<td>Triethanolamine</td>
<td>1.2%</td>
</tr>
<tr>
<td>Glycerin</td>
<td>34.2%</td>
</tr>
<tr>
<td>Propylene Glycol</td>
<td>2.0%</td>
</tr>
<tr>
<td>Dimethicone copolyol</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

Prepare the carbomer gel, add the other ingredients, and mix well. Dimethicone copolyol is included to reduce the sticky feel associated with glycerin.

Poloxamer Gel Base

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pluronic F-127, NF</td>
<td>20 g-50 g</td>
</tr>
<tr>
<td>Purified Water/Buffer qs</td>
<td>100 mL</td>
</tr>
</tbody>
</table>

PRESERVATION OF GELS

Many gels will not promote bacterial or mold growth nor will they prevent it. Consequently, they need to be autoclaved or contain preservatives. Table 3 lists a number of preservatives and concentrations that have been used in the preparation of gels.

GENERAL DISCUSSION

In gel preparation, the powdered polymers, when added to water, may form temporary gels that slow the process of dissolution. As water diffuses into these loose clumps of powder, their exteriors frequently turn into clumps of solvated particles encasing dry powder. The blobs of gel dissolve very slowly because of their high viscosity and low diffusion coefficient of the macromolecules.

As a hot, colloidal dispersion of gelatin cools, the gelatin macromolecules lose kinetic energy. With reduced kinetic energy, or thermal agitation, the gelatin macromolecules are associated through dipole-dipole interaction into elongated or threadlike aggregates. The size of these association chains increases to the extent that the dispersing medium is held in the interstices among the interfacing network of gelatin macromolecules, and the viscosity increases to that of a semisolid. Gums, such as agar, Irish moss, algin, pectin and tragacanth, form gels by the same mechanism as gelatin.

Polymer solutions tend to cast gels because the solute consists of long, flexible chains of molecular thickness that tend to become entangled, attract each other by secondary valence forces, and even crystallize. Crosslinking of dissolved polymer molecules also causes the solutions to gel. The reactions produce permanent gels, held together by primary valence forces. Secondary valence forces are responsible for reversible gel formation. For example, gelatin will form a gel when lowered to about 30°C, the gel melting point, but aqueous methylcellulose solutions will gel when heated above about 50°C because the polymer is less soluble in hot water and precipitates. Lower temperatures, higher concentrations and higher molecular weights promote gelation and produce stronger gels. The reversible gelation of gelatin will occur at about 25°C for 10% solutions, 30°C for 20% solutions and about 32°C for 30% solutions. Gelation is rarely observed for gelatin above 34°C and, regardless of concentration, gelatin solutions do not gel at 37°C. The gelation temperature or gel point of gelatin is highest at the isoelectric point. Water soluble polymers have the property of thermal gelation, i.e., they gel on heating, whereas natural gums gel on cooling. Thermal gelation is reversed on cooling.

Inorganic salts will compete with the water present in a gel and cause gelation to occur at lower concentrations. This is usually a reversible process and, upon the addition of water, the gels will re-form. Alcohol may cause precipitation or gelation because alcohol is a nonsolvent or precipitant, lowering the dielectric constant of the medium and tending to dehydrate the hydrophilic solute. Alcohol lowers the concentrations at which electrolytes salt out hydrophilic colloids. Phase separation by adding alcohol may cause coacervation.

Aqueous polymer solutions, especially of cellulose derivatives, are stored for approximately 48 hours after dissolution to promote full hydration, maximum viscosity and clarity. If salts are to be added, they are incorporated at this point rather than by dissolving in the water prior to adding the polymer; otherwise the solutions may not reach their full viscosity and clarity.

SUMMARY

Gels provide the pharmacist with an excellent drug delivery system for different routes of administration and are compatible with many different substances. Gels containing penetration enhancers are especially popular for administering anti-inflammatory and antinauseant medications. They are relatively easy to prepare and are very efficacious.