Stabilising and Suspending Agents

The stabilising and suspending agents described in this chapter have the property of increasing the viscosity of water when dissolved or dispersed. The rheological properties of the dispersions can vary widely from thin liquids to thick gels.

They have wide applications both in pharmaceutical manufacturing and in the food industry. As well as being used as thickening and suspending agents many are used in emulsions as stabilisers and in some cases as emulsifying agents; some are also used in the manufacture of tablets as disintegrants, binding and granulating agents, and for film or enteric coating.

Some are used in artificial tear and artificial saliva preparations which are used in the management of dry eye and dry mouth respectively. Those most commonly used are carbomers, cellulose ethers such as carmellose and hypromellose, polyvinyl alcohol, and povidone. Some, such as the alginates and methylcellulose, are also used in gastrointestinal disorders.

Dry eye

Dry eye is a chronic condition caused by instability of the tear film covering the eye; the tear film breaks up to leave dry spots rather than being maintained between blinks. Tears consist of a slightly alkaline fluid that is spread across the eye by blinking and is lost via the lachrymal ducts or by evaporation. Mucus secreted by the conjunctiva is also required to maintain tear film stability and dry eye can result from reduced production of either tears or conjunctival mucus. Reduced tear secretion is common in the elderly, but also occurs in some systemic disorders or as an adverse effect of drugs such as those, like tricyclic antidepressants, that have antimuscarinic effects. Tear film instability may also result from increased tear evaporation, for example due to corneal exposure in thyroid disease, or from lid, corneal, or other eye disorders.

The main symptoms of dry eye are discomfort, typically with a chronic gritty sensation, visual disturbances, and sometimes photophobia. If left untreated corneal ulceration and eventual loss of sight may occur. Keratoconjunctivitis sicca (corneal inflammation) may result from severe dry eye in Sjögren's syndrome (see below).

Treatment of dry eye is primarily symptomatic using 'artificial tears' preparations; eye drops containing hypromellose or other cellulose ethers (carmellose, hyetellose, methylcellulose), polyvinyl alcohol, or povidone are used. Carbomer, in liquid gel formulations, and ointments containing soft or liquid paraffins are also used. Ointments have a longer duration of action than drops, but tend to blur the vision and are most suitable for use at night. Drops should be used as frequently as required, up to hourly or more often if necessary. Frequent use of eye drops may cause sensitivity to the preservative, in which case preservative-free preparations should be considered. An alternative in patients needing very frequent instillation of drops is a slow-release ophthalmic insert of hyprolose. Punctal occlusion with gelatin rods or collagen implants is used diagnostically to block tear outflow and treatment by permanent occlusion may be considered. Mucus build-up due to reduced tear production may respond to topical mucolytics such as acetylcysteine or bromhexine. Topical immunosuppressants such as ciclosporin may be of benefit in some patients with keratoconjunctivitis sicca;[1] combination of topical ciclosporin with punctal occlusion has been tried.[2]

Sjögren's syndrome is an auto-immune inflammatory disease primarily affecting the lachrymal and salivary glands, and manifests as dry eye and dry mouth. It is often secondary to an auto-immune disorder such as rheumatoid arthritis.[3] Treatment is mainly symptomatic[4] using artificial tears and topical mucolytics for dry eye; dry mouth is treated with artificial saliva as outlined below. Oral pilocarpine may be of benefit for both dry eye and dry mouth;[5,6] systemic treatment with the mucolytic bromhexine has produced conflicting results.[7-9] Corticosteroids and immunosuppressants may have a role in patients with CNS involvement.[10]

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Dry mouth

Dryness of the mouth (xerostomia) resulting from decreased salivary secretion is often an adverse effect of therapy with drugs such as antimuscarinics, antihistamines, tricyclic antidepressants, and diuretics. Other causes include dehydration, anxiety, Sjögren's syndrome (see Dry Eye, above), and radiotherapy of the head and neck. Dry mouth can cause eating difficulties and lead to oral disease such as candidiasis, dental caries, and bacterial infections.[1,2] Where possible any underlying disorder should be treated first.

Frequent sips of fluids help to relieve dry mouth. Artificial saliva products are also important in the symptomatic treatment of dry mouth. They aim to mimic normal saliva and generally contain viscosity-increasing agents, such as mucins or cellulose derivatives such as carmellose,[3,4] as well as electrolytes, including fluoride; they seldom relieve symptoms for more than 1 or 2 hours. It may be possible to stimulate saliva production with sialogogues such as sugarless chewing gum or citrus products but the low pH of the latter can damage the teeth. Malic acid has also been used as a sialogogue.

A number of systemic therapies have also been tried. Pilocarpine is an effective sialogogue, increasing salivary production where some function remains,[5] and is used in dry mouth following radiotherapy; it may also be effective in Sjögren's syndrome or other causes of dry mouth. Adverse effects, particularly increased sweating, may, however, limit its use.[6] Carbachol has been suggested as an alternative to pilocarpine with a study[7] reporting comparable efficacy but less sweating. Anethole trithione and cevimeline have been used similarly. Amifostine is used for the prevention of dry mouth associated with radiotherapy.

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Acacia

Acac.; Acaciae gummi; Akaasiakumi; Akaciagummi; Arabmézga; Arabská klovatina; E414; Goma arábiga; Gomme arabique; Gomme de Sénégal; Gum Acacia; Gum Arabic; Guma arabska; Gumiarabikas; Gummi Africanum; Gummi Arabicum; Gummi Mimosae.

CAS — 9000-01-5.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *Jpn.* Also in *USNF.*

Ph. Eur. 6.2 (Acacia). The air-hardened gummy exudate from the trunk and branches of *Acacia senegal*, other species of *Acacia* of African origin, and *Acacia seyal*. Yellowish-white, yellow, or pale amber tears, sometimes with a pinkish tint. It is friable, opaque, frequently with a cracked surface, easily broken into irregular, whitish or slightly yellowish angular fragments with conchoidal fracture and a glassy and transparent appearance. Very slowly but almost completely soluble, after about 2 hours, in twice its mass of water leaving only a very small residue of vegetable particles; the liquid obtained is colourless or yellowish, dense, viscous, adhesive, translucent, and weakly acid to blue litmus paper. Practically insoluble in alcohol. Protect from light.

Ph. Eur. 6.2 (Acacia, Spray-dried; Acaciae Gummi Dispersione Desiccatum). It is obtained from a solution of acacia. Dissolves, rapidly and completely, after about 20 minutes, in twice its mass of water. The liquid obtained is colourless or yellowish, dense, viscous, adhesive, translucent, and weakly acid to blue litmus paper. Practically insoluble in alcohol. Protect from light.

USNF 26 (Acacia). The dried gummy exudate from the stems and branches of *Acacia senegal* (Leguminosae) or of other related African species of *Acacia*. Spheroidal tears or angular fragments of white to yellowish-white colour. It is translucent or somewhat opaque from the presence of numerous minute fissures. It is very brittle, the fractured surface is glassy and occasionally iridescent. It is also available as flakes, powder, granules, or as a spray-dried form. It is practically odourless. Insoluble in alcohol. Store in airtight containers.

Incompatibility. Incompatibilities of acacia have been reported with a number of substances including alcohol, aminophenazone, apomorphine, cresol, ferric salts, morphine, phenol, physostigmine, tannins, thymol, and vanillin. Acacia contains an oxidising enzyme that may affect preparations containing easily oxidised substances; the enzyme may be inactivated by heating at 100° for a short time.

Adverse Effects

Hypersensitivity reactions have occurred rarely after inhalation or ingestion of acacia.

Uses

Acacia is used in pharmaceutical manufacturing as a suspending and emulsifying agent, as a tablet binder, and in pastilles. It is often used with tragacanth.

It is used as an emulsifier and stabiliser in the food industry.

Preparations

USNF 26: Acacia Syrup.

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Indon.:*** Norflam.

Agar

Agar-agar; Agaras; Colle du Japon; E406; Gelosa; Gélose; Japanese Isinglass; Layor Carang.

CAS — 9002-18-0.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn.* Also in *USNF.*

Ph. Eur. 6.2 (Agar). Polysaccharides extracted from various species of Rhodophyceae algae, mainly those belonging to the genus *Gelidium*. It is prepared by treating the algae with boiling water; the extract is filtered while hot, concentrated, and dried. Colourless to pale yellow translucent strips, flakes, or powder; tough when damp but becoming more brittle on drying.

USNF 26 (Agar). The dried, hydrophilic, colloidal substance extracted from *Gelidium cartilagineum* (Gelidiaceae), *Gracilaria confervoides* (Sphaerococcaceae), and related red algae (Class Rhodophyceae). It usually consists of thin, membranous, agglutinated strips, but may occur in cut, flaked, or granulated forms. May be weak yellowish-orange, yellowish-grey to pale yellow, or colourless. It is tough when damp, brittle when dry. Odourless or has a slight odour. Insoluble in cold water; soluble in boiling water.

Uses and Administration

Agar is used as a suspending or thickening agent in pharmaceutical manufacturing and as an emulsifying and stabilising agent in the food industry.

It was formerly used similarly to methylcellulose (p.2145) as a bulk laxative. Preparations containing agar with liquid paraffin and phenolphthalein are available to treat constipation, but the relatively small amount of agar in these probably acts solely as an emulsion stabiliser.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Agarol; Usar Fibras†; ***Austral.:*** Lexat†; ***Braz.:*** Agarol; Fenogar†; ***Chile:*** Agarol; ***Fr.:*** Pseudophage; ***India:*** Agarol†; ***Port.:*** Byl†; ***Switz.:*** Paragar; ***USA:*** Agoral; ***Venez.:*** Agarol†.

Alginic Acid

Acide alginique; Acidum alginicum; Algiinihappo; Algínico, ácido; Algino rūgštis; Alginsav; Alginsyra; Aljinik Asit; E400; Kyselina alginová; Polymannuronic Acid.

CAS — 9005-32-7.

ATC — A02BX13.

ATC Vet — QA02BX13.