

a higher incidence of stroke in a group of patients given doses of 500 micrograms compared with a group receiving 300 micrograms. Patients with a history of stroke appeared to be at greater risk.

Uses and Administration

Ranibizumab is a recombinant humanised monoclonal antibody used in the treatment of neovascular (wet) age-related macular degeneration. It is given by intravitreal injection into the affected eye in doses of 500 micrograms once a month initially for 3 to 4 months. In the UK, after the first 3 months, maintenance treatment is based on regular assessment of visual acuity, with ranibizumab being given if the patient had a loss of greater than 5 letters in visual acuity; the interval between consecutive doses should be at least one month. In the USA, if monthly administration is not feasible after the first four injections, treatment may be given once every 3 months, although this is not as effective as monthly doses.

Age-related macular degeneration. Ranibizumab is a recombinant humanised monoclonal antibody fragment related to bevacizumab (p.684) used in the treatment of (wet) age-related macular degeneration (AMD) (p.785). It binds to and inhibits vascular endothelial growth factor A (VEGF-A), which is a stimulant of angiogenesis thought to play a role in the neovascularisation and retinal changes associated with AMD. Ranibizumab inhibits all active forms of VEGF-A.¹

Positive outcomes have been reported from two international multicentre randomised controlled phase III studies.^{2,3} Vision loss was prevented and mean visual acuity improved in patients given either monthly injections of 300 micrograms or 500 micrograms for 2 years compared with patients receiving sham injections.² Ranibizumab given in the same doses was also shown to be superior to photodynamic therapy with verteporfin at 1 year in the second study.³

A review⁴ of interim results of other ongoing phase III studies of ranibizumab for AMD suggests that reducing the dosing interval to once every 3 months is less satisfactory than monthly injections, although tailoring the treatment to morphological parameters was as effective at 1 year as giving a fixed dosage regimen. However, ranibizumab in combination with photodynamic therapy does not necessarily result in better visual acuity outcomes and may even be worse than ranibizumab alone. A systematic review⁵ of 5 randomised controlled studies found that ranibizumab was effective in reducing the risk of loss of visual acuity, and also improved visual acuity in a significant proportion of eyes.

1. Blick SKA, *et al.* Ranibizumab. *Drugs* 2007; **67**: 1199–1206.
2. Rosenfeld PJ, *et al.* for the MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006; **355**: 1419–31.
3. Brown DM, *et al.* for the ANCHOR Study Group. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *N Engl J Med* 2006; **355**: 1432–44.
4. Rosenfeld PJ, *et al.* Ranibizumab: phase III clinical trial results. *Ophthalmol Clin North Am* 2006; **19**: 361–72.
5. Vedula SS, Krzystolik MG. Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 06/06/08).

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Lucentis; **Cz.:** Lucentis; **Fr.:** Lucentis; **Gr.:** Lucentis; **Indon.:** Lucentis; **Malaysia:** Lucentis; **Port.:** Lucentis; **UK:** Lucentis; **USA:** Lucentis.

Rapeseed Oil

Colza, aceite de; Colza, huile de; Colza Oil; Olej rzepakowy; Oleum Rapae; Rapae oleum; Rape Oil; Rapsolja; Rapsuj alejus; Repceolaj; Repkový olej; Rypsiölj.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn. USNF* includes fully hydrogenated rapeseed oil and superglycerinated fully hydrogenated rapeseed oil.

Ph. Eur. 6.2 (Rapeseed Oil, Refined). The fatty oil obtained from the seeds of *Brassica napus* and *Brassica campestris* by mechanical expression or extraction and then refined. A suitable antioxidant may be added. It contains not more than 2% of erucic acid. A clear light yellow liquid. Practically insoluble in water and in alcohol; miscible with petroleum spirit. Store in well-filled airtight containers. Protect from light.

USNF 26 (Fully Hydrogenated Rapeseed Oil). A mixture of triglycerides in which the fatty acid composition is a mixture of saturated fatty acids. It is obtained by refining and hydrogenating oil obtained from the seeds of *Brassica napus* and *Brassica campestris*. It contains not more than 1% of erucic acid. A white, waxy solid. Insoluble in water and in alcohol. Store in airtight containers. Protect from light.

USNF 26 (Superglycerinated Fully Hydrogenated Rapeseed Oil). A mixture of mono-, di-, and triglycerides, with triglycerides as a minor component. It is obtained by refining, hydrogenating, and glycerinating oil obtained from the seeds of *Brassica napus* and *Brassica campestris*. It contains not more than 1% of erucic acid. A white solid. Insoluble in water and in alcohol. Store in airtight containers. Protect from light.

Profile

Rapeseed oil has been used in liniments in place of olive oil. It is used in some countries as an edible oil but the erucic acid (C₂₂H₄₂O₂ = 338.6) content of the oil has been implicated in muscle damage. The erucic acid content of oils and fats intended for human consumption and of foodstuffs containing oil or fat is subject to legal control. Contaminated rapeseed oil was the cause of the toxic oil syndrome that affected thousands of Spanish citizens in early 1981. Rapeseed oil is also used in industrial manufacturing.

There has been some debate whether the frequency of allergic respiratory symptoms in sensitive individuals is increased in areas in which oilseed rape is cultivated.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient. Gr.: Fissan-Pate†.

Raspberry Leaf

Frambuesa, hoja de; Rubi Idaei Folium.

Profile

Raspberry leaf consists of the dried leaflets of *Rubus idaeus* (Rosaceae). It contains a principle, readily extracted with hot water, which relaxes the smooth muscle of the uterus and intestine of some animals.

Raspberry 'tea' has been a traditional remedy for painful and profuse menstruation and for use before and during labour. The infusion has also been used as an astringent gargle.

References

1. Simpson M, *et al.* Raspberry leaf in pregnancy: its safety and efficacy in labor. *J Midwifery Womens Health* 2001; **46**: 51–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient. Austral.: Rubus Complex†; **Cz.:** Detsky Caj s Hermanem; Diabetan; Hertz- und Kreislauffeje†; Hypotonicka; Species Chologogae Planta.

Relaxin

Relaxina.
CAS — 9002-69-1.

Profile

Relaxin is a polypeptide hormone that has been extracted from the corpus luteum of the ovaries of pregnant sows, although a human recombinant form is also now available. It is reported to be related structurally to insulin and has a molecular weight of about 6000.

Relaxin is secreted by the human corpus luteum during pregnancy and is thought to interact with other reproductive hormones. It acts on connective tissue, including collagen, and causes relaxation of the pubic symphysis and softening of the uterine cervix. In many animal species relaxin appears to play a major part in cervical ripening before parturition; significant species difference is shown. It has been studied for cervical ripening in humans. Recombinant human relaxin has also been investigated in infertility, cardiovascular disorders, and scleroderma (p.1817).

References

1. Seibold JR, *et al.* Safety and pharmacokinetics of recombinant human relaxin in systemic sclerosis. *J Rheumatol* 1998; **25**: 302–7.
2. Seibold JR, *et al.* Recombinant human relaxin in the treatment of scleroderma: a randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 2000; **132**: 871–9.
3. Kelly AJ, *et al.* Relaxin for cervical ripening and induction of labour. Available in The Cochrane Database of Systematic Reviews; Issue 2. John Wiley; Chichester; 2001 (accessed 28/04/06).

Resveratrol

NSC-327430; 3,4',5-Stilbenetriol; 3,4',5-Trihydroxystilbene. (E)-5-[2-(4-Hydroxyphenyl)ethenyl]-1,3-benzenediol.

C₁₄H₁₂O₃ = 228.2.
CAS — 501-36-0.

Profile

Resveratrol is a phytoalexin present in a range of plant sources including species of *Arachis*, *Pinus*, *Polygonum*, *Veratrum*, and *Vitis*. It is thought to be one of the compounds responsible for the cardioprotective action of wine (see Grape, p.2316, and Flavonoid Compounds, p.2304).

Resveratrol used in commercial preparations is often derived from the root of Japanese knotweed, *Fallopia japonica* (*Polygonum cuspidatum*; *Reynoutria japonica*) (Polygonaceae) often as the racemate although the *trans*-isomer is also promoted.

Resveratrol is promoted as an antioxidant for the prevention of atherosclerosis. It also has mixed agonist/antagonist activity at oestrogen receptors and some anti-inflammatory and antiproliferative activity, and is under investigation in the prevention and treatment of malignancy.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Resvelief†.

Rhamnose

Rammosa; Ramnoza; L-Rhamnose. 6-Deoxy-L-mannose.

C₆H₁₂O₅ = 164.2.
CAS — 3615-41-6.

Profile

Rhamnose is a monosaccharide used to assess intestinal permeability.

For reference to the use of rhamnose in the differential sugar absorption test, see Diagnosis and Testing under Lactulose, p.1739.

References

1. van Nieuwenhoven MA, *et al.* The sensitivity of the lactulose/rhamnose gut permeability test. *Eur J Clin Invest* 1999; **29**: 160–5.
2. Haase AM, *et al.* Dual sugar permeability testing in diarrheal disease. *J Pediatr* 2000; **136**: 232–7.
3. van Nieuwenhoven MA, *et al.* Effects of pre- and post-absorptive factors on the lactulose/rhamnose gut permeability test. *Clin Sci* 2000; **98**: 349–53.

Rhatany Root

Krameria; Krameria Root; Ratanhia, racine de; Ratanhia radix; Ratanhiagyökér; Ratanhový kořen; Ratania, raíz de; Ratanianjuuri; Rataniarot; Ratanijü šaknys.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Rhatany Root). The dried, usually fragmented, underground organs of *Krameria triandra*. It contains not less than 5% of tannins, expressed as pyrogallol, calculated with reference to the dried drug. It is known as Peruvian rhatany. Protect from light.

Profile

Rhatany root has astringent properties and is used in herbal preparations for a variety of disorders, including oropharyngeal inflammation.

Homoeopathy. Rhatany root has been used in homoeopathic medicines under the following names: Ratanhia; Krameria triandra; Ratanhia radix; Ratania perviana; Ratan.

Preparations

Ph. Eur.: Rhatany Tincture.

Proprietary Preparations (details are given in Part 3)

Ger.: ratioSept.

Multi-ingredient. Arg.: Esculeol P; Parodontax Fluor; **Austria:** Parodontax; **Braz.:** Malvatricin Natural Organic; Parodontax; **Chile:** Hemorrolf; **Fr.:** Delabarre Bio-adhesif; **Ger.:** Ratanhia comp; Repha-Os; **Israel:** Parodontax†; **Ital.:** Gengivario†; **Spain:** Encialina†; **Switz.:** Eubucal†; GU Eau†; Parodontax F†; Parodontax†; Sanogencive.

Rhus

Sumach Berries; Zumaque.

Pharmacopoeias. *Br.* includes Toxicodendron Quercifolium for Homoeopathic Preparations.

BP 2008 (Toxicodendron Quercifolium for Homoeopathic Preparations). Fresh, young, not yet lignified shoots, with leaves, of *Toxicodendron quercifolium*. The shoots contain a yellowish-white milky sap that is a strong cutaneous irritant and darkens the skin. Contact with the skin and mucous membranes is to be avoided.

Profile

Rhus consists of the dried fruits of the smooth or Pennsylvanian sumach, *Rhus glabra* (Anacardiaceae). It has astringent and reputed diuretic properties. *R. aromatica* has been used similarly to *R. glabra*.

Poison ivy (*R. radicans*) and poison oak (*R. toxicodendron*), species growing in the USA, contain irritant poisons, such as urushiol, that produce severe contact dermatitis. Extracts of poison ivy and poison oak have been used for the prophylaxis of poison ivy dermatitis but their effectiveness has not been proved. The spice sumac is prepared from the berries of *R. coriaria*.

Homoeopathy. Some *Rhus* spp. are used in homoeopathic medicine. Poison oak has been used in homoeopathic medicines under the following names: Toxicodendron quercifolium; Rhus toxicodendron; Rhus. tox.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient. Austral.: Joint & Muscle Cream; **Chile:** Rhus Opodeldoc; **Ger.:** Hicoton†; Rhus-Rheuma-Gel N.

Ribonuclease

Ribonucleasa; RNase.

CAS — 9001-99-4.

Profile

Ribonuclease is an enzyme present in most mammalian tissue, and it is involved in the catalytic cleavage of ribonucleic acid. It