2. Weeks GR, Proper JS. Herbal medicines—gaps in our knowledge. *Aust J Hosp Pharm* 1989; **19:** 155–7.
3. Shaw HS, *et al.* Delayed-type hypersensitivity reaction with Iscador M given in combination with cytotoxic chemotherapy. *J Clin Oncol* 2004; **22:** 4432–4.

Malignant neoplasms. Reviews[1-3] of the use of mistletoe for the treatment of malignant neoplasms revealed that studies have been of variable quality, and have produced conflicting results; it has been suggested that the more rigorous studies do not show benefit.[3] A systematic review[4] of 21 randomised controlled studies found major methodological flaws in most of the studies and concluded that there was insufficient evidence to provide guidelines for the use of mistletoe extracts in oncology.

1. Mansky PJ. Mistletoe and cancer: controversies and perspectives. *Semin Oncol* 2002; **29:** 589–94.
2. Kienle GS, *et al.* Mistletoe in cancer—a systematic review on controlled clinical trials. *Eur J Med Res* 2003; **8:** 109–19.
3. Ernst E, *et al.* Mistletoe for cancer? A systematic review of randomised clinical trials. *Int J Cancer* 2003; **107:** 262–7.
4. Horneber MA, *et al.* Mistletoe therapy in oncology. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 03/06/08).

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Eurixor; Helixor; Iscador; Isorel; ***Cz.:*** Nat Jmeli; ***Ger.:*** Abnobaviscum; Cefalektin; Eurixor; Helixor; Iscador; Lektinol; Mistel Curarina; Mistel-Krautertabletten; Mistelol-Kapseln†; Misteltropfen Hofmanns; Misteltropfen†; Salus Mistel-Tropfen; Viscysat; ***Switz.:*** Iscador.

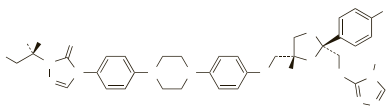
Multi-ingredient: ***Austral.:*** Calmo; Pacifenity†; ***Austria:*** Rutiviscal; Wechseltee St Severin; ***Cz.:*** Alvisan Neo; Hypotonicka; ***Fr.:*** Mediflor Tisane Circulation du Sang No 12; ***Ger.:*** Antihypertonicum S; Asgoviscum N†; Heusin†; Hypercircin; Ilja Rogoff; Presselin Arterien K 5 P†; Syviman N†; Viscophyll†; ***Pol.:*** Cravisol; Venoforton; ***Rus.:*** Herbion Drops for the Heart (Гербион Сердечные Капли).

Mitratapide *(USAN, rINN)*

Mitratapid; Mitratapida; Mitratapidum; R-103757. 2-[(2*R*)-Butan-2-yl]-4-(4-{4-[4-({(2*S*,4*R*)-2-(4-chlorophenyl)-2-[(4-methyl-4*H*-1,2,4-triazol-3-ylsulfanyl)methyl]-1,3-dioxolan-4-yl}methoxy)-phenyl]piperazin-1-yl}phenyl)-2,4-dihydro-3*H*-1,2,4-triazol-3-one.

Митратапид

$C_{36}H_{41}ClN_8O_4S$ = 717.3.
CAS — 179602-65-4.
ATC Vet — QA08AB90.



Profile

Mitratapide is an inhibitor of the microsomal triglyceride transfer protein. It is used in veterinary medicine as an aid to management of obesity in *dogs*.

Monoctanoin *(BAN, USAN)*

Monoctanoína; Monooctanoin; Mono-octanoin.
CAS — 26402-26-6 (glyceryl mono-octanoate).

Description. Monoctanoin is a semisynthetic mixture of glycerol esters, containing 80 to 85% of glyceryl mono-octanoate ($C_{11}H_{22}O_4$ = 218.3), 10 to 15% of glyceryl mono-decanoate ($C_{13}H_{26}O_4$ = 246.3) and glyceryl di-octanoate ($C_{19}H_{36}O_5$ = 344.5), and a maximum of 2.5% of free glycerol ($C_3H_8O_3$ = 92.09).

Profile

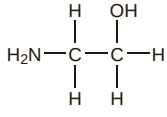
Monoctanoin given by continuous perfusion through a catheter inserted directly into the common bile duct has been used to dissolve cholesterol gallstones (p.2409) retained after cholecystectomy.

Preparations

Proprietary Preparations (details are given in Part 3)
USA: Moctanin†.

Monoethanolamine

2-Hydroxyethylamine; 2-Aminoethanol.
C_2H_7NO = 61.08.
CAS — 141-43-5.



Pharmacopoeias. In *Br.* Also in *USNF.*
BP 2008 (Ethanolamine). A clear, colourless, or pale yellow liquid with a slight odour. It is alkaline to litmus. Miscible with water and with alcohol; slightly soluble in ether.
USNF 26 (Monoethanolamine). A clear, colourless, moderately viscous liquid having a distinctly ammoniacal odour. Miscible with water, with alcohol, with acetone, with chloroform, and with glycerol; immiscible with ether, with petroleum spirit, and with fixed oils, although it dissolves many essential oils. Store in airtight containers. Protect from light.

Monoethanolamine Oleate *(rINN)*

Ethanolamine Oleate *(USAN)*; Monoéthanolamine, Oléate de; Monoethanolamini Oleas; Oleato de monoetanolamina. 2-Hydroxyethylamine compound with oleic acid; 2-Aminoethanol compound with oleic acid.

Моноэтаноламина Олеат
$C_2H_7NO,C_{18}H_{34}O_2$ = 343.5.
CAS — 2272-11-9.
ATC — C05BB01.
ATC Vet — QC05BB01.

Adverse Effects and Precautions

Monoethanolamine oleate is irritant to skin and mucous membranes. Local injection may cause sloughing, ulceration, and, in severe cases, necrosis. Pain may occur at the site of injection. Patients receiving treatment for oesophageal varices may develop pleural effusion or infiltration. Hypersensitivity reactions have been reported.

Sclerotherapy should not be used to treat varicose veins of the legs in patients unable to walk, with obese legs, with thrombosis or a tendency to thrombosis, or with acute phlebitis, marked arterial, cardiac, or renal disease, local or systemic infections, or uncontrolled metabolic disorders such as diabetes mellitus. Monoethanolamine oleate should not be used in patients taking oral contraceptives.

Effects on the kidneys. Acute renal failure, which cleared spontaneously within 3 weeks, occurred in 2 obese women given sclerosing injections of 15 to 20 mL of a solution containing monoethanolamine oleate 5% and benzyl alcohol 2%.[1]

1. Maling TJB, Cretney MJ. Ethanolamine oleate and acute renal failure. *N Z Med J* 1975; **82:** 269–70.

Uses and Administration

Monoethanolamine oleate is used as a sclerosant in the treatment of varicose veins and oesophageal varices. For sclerotherapy of varicose veins, 2 to 5 mL of a 5% solution of monoethanolamine oleate is injected slowly into empty isolated sections of vein, divided between 3 or 4 sites. Injection into full veins is also possible. For sclerotherapy of oesophageal varices, the dose is 1.5 to 5 mL of a 5% solution per varix to a maximum total dose of 20 mL per treatment session. Treatment may be given in the initial management of bleeding varices, then repeated at intervals until the varices are occluded.

Variceal haemorrhage. Portal hypertension may occur in many conditions that affect the liver, and leads to the development of collateral channels linking the portal and systemic circulations. Enlargement of such blood vessels beneath the oesophageal and gastric mucosa produces varices which have about a 30% risk of rupture and bleeding. Oesophageal varices are more often a cause of haemorrhage than gastric varices. Capillaries and veins in the gastric mucosa may also become swollen, a condition known as portal hypertensive gastropathy, and clinically important bleeding may occur in severe cases.

Variceal haemorrhage is usually severe, with mortality as high as 50% for the initial episode; the recurrence rate may be as high as 100% in patients who survive without treatment. Bleeding may stop spontaneously, but in those who continue to bleed, control of haemorrhage is difficult and patients should be referred to a centre with appropriate specialist facilities. Treatment to stabilise the patient may be necessary before they can be safely transferred.

Acute management. Initial treatment is supportive and requires measures to prevent aspiration and maintain a clear airway, and volume replacement with colloid and blood. Emergency endoscopy should be performed to establish the site of haemorrhage and exclude non-variceal sources of bleeding. The choice of treatment depends on the site of haemorrhage.[1-9] ***Endoscopic methods*** have been favoured for initial management. Injection sclerotherapy or banding ligation are used for bleeding oesophageal varices but the optimum management of bleeding gastric varices remains to be defined; the value of injection sclerotherapy varies with their location. Intravariceal injection of bovine or human thrombin, or cyanoacrylate tissue adhesives, has been used in gastric varices. Where the source of haemorrhage is non-variceal and due to gastropathy, portal decompressive surgery is effective, although it is associated with a high incidence of encephalopathy in cirrhotic patients. Small studies have shown propranolol to be effective in arresting haemorrhage.[10]

Injection sclerotherapy for variceal haemorrhage may be performed during the emergency endoscopy procedure. Intravariceal injection, paravariceal injection, or a combination of the two have been used. The most widely used sclerosants are monoethanolamine oleate and sodium tetradecyl sulfate for intravariceal injection and lauromacrogol 400 for paravariceal injection. Sclerotherapy controls bleeding in up to 95% of cases. Ulceration and stricture formation occur frequently following injection sclerotherapy.

An alternative technique is ***endoscopic banding ligation***, where elastic bands are placed around the varices. The tissue subsequently necroses to leave a superficial ulcer. This technique is more successful than injection sclerotherapy, but may be more difficult to perform if active bleeding is occurring. Procedures may be repeated if bleeding continues or restarts.

Where endoscopy is unavailable, drug therapy or balloon tamponade may be used until the patient can be transferred to a specialist centre. These techniques may also have a role when sclerotherapy fails and some have suggested that initial drug therapy may be preferable to sclerotherapy[11] or endoscopy.[12]

Drug therapy is aimed at controlling portal venous pressure, although it is ineffective in massive haemorrhage and its effects cease once the drug is stopped. Two meta-analyses[11,13] have examined data from studies comparing drug therapy with endoscopic methods for the treatment of acute variceal bleeding. Sclerotherapy did not appear to be superior to vasoactive drugs as the first single treatment, and was associated with more frequent adverse effects.[11] Adjunctive drug therapy improved the efficacy of endoscopic therapy (injection sclerotherapy or band ligation) compared with endoscopic methods alone, although overall mortality was not affected; severe adverse effects were similar in both groups.[13]

Drugs used include vasopressin and its analogue terlipressin and, more recently, somatostatin and its analogue octreotide. Vasopressin controls haemorrhage in about 50% of patients. It is given by continuous intravenous infusion, together with glyceryl trinitrate, which counteracts the adverse cardiac effects of vasopressin, while potentiating its reduction of portal pressure. Terlipressin has the advantage of a longer therapeutic action, enabling bolus doses to be given. A comparison[14] of terlipressin and sclerotherapy found them to be equally effective for the control of acute variceal bleeding. A systematic review[15] of studies comparing terlipressin with placebo, or other drugs or interventions, also gave favourable results. However, somatostatin,[2] and particularly octreotide,[2,16,17] which may be given by bolus injection, are now generally preferred as they are thought to have similar efficacy to vasopressin but fewer adverse effects. A meta-analysis[18] of studies comparing somatostatin or its analogues octreotide and vapreotide with either placebo or no drug treatment suggested a small benefit in controlling bleeding; however, no mortality benefit has yet been shown. Clinical studies with recombinant factor VIIa to control acute variceal bleeding have produced beneficial results.[12]

Balloon tamponade controls bleeding by direct pressure on the varices. Although it is a very effective means of controlling haemorrhage, there is a high incidence of rebleeding once pressure is removed and the incidence of complications is high. It is useful in cases of massive haemorrhage when drug therapy is ineffective and sclerotherapy is difficult.

Surgery, such as the formation of a shunt or oesophageal transection, may be necessary if the above measures fail to control the bleeding. However, such techniques have been associated with high mortality in some series. Formation of a transjugular intrahepatic portal-systemic shunt (TIPS) is now generally preferred.[4] It may be particularly useful in candidates for liver transplantation. Limited data suggest that the shunt may remain patent in the majority of patients for at least 3 years.[19]

Short-term ***antibacterial prophylaxis*** has been proposed[20] for cirrhotic patients with gastrointestinal bleeding, including variceal bleeding, because reduced rates of infection and improved short-term survival have been reported in a few studies, although there is no benefit on overall mortality.[21]

Long-term management. Once the acute bleeding has been controlled measures are needed to prevent rebleeding. Endoscopic therapy is widely used, with injection sclerotherapy or banding ligation being repeated until the varices are obliterated. Banding ligation is now the treatment of choice; it eradicates varices in fewer treatment sessions than injection sclerotherapy and reduces the risk of ulceration and stricture formation.[22,23] Sucralfate has been given following sclerotherapy as it may reduce the frequency of stricture formation and reduce bleeding from treatment-related ulcers. It seems to have no influence on ulcer healing following banding ligation.[24] Some practitioners carry out regular endoscopic checks and repeat sclerotherapy or banding ligation when varices reappear, although this approach is no more effective in terms of improving survival than giving treatment once bleeding occurs. Drug therapy is an alternative to endoscopic methods.[25] Beta blockers (mainly propranolol) reduce the incidence of recurrent variceal bleeding and may improve survival.[23,26,27] A combination of nadolol with isosorbide mononitrate has been reported to reduce the risk of rebleeding more than repeated sclerotherapy, although there was no significant effect on mortality.[28] Drug therapy has also been used as an adjunct to endoscopic methods to control rebleeding in the period before variceal obliteration has occurred, or for long-term management following endoscopic therapy. However, studies comparing endoscopic band ligation with combination drug therapy have produced variable results.[29] Long-term octreotide therapy following sclerotherapy has also been investigated and may reduce recurrent variceal bleeding.[30] Several studies[31-33] have compared TIPS with endoscopic treatment, but no clear benefit has been demonstrated and there may be an increased risk of encephalopathy with the use of shunts. Surgery, including liver transplantation, should be considered in patients with recurrent