Stroke. Gavestinel has been tried for its supposed neuroprotective properties in acute stroke, but two major multicentre, randomised controlled studies have failed to show any benefit over placebo in acute ischaemic stroke.[1,2] Analysis of the data from these two studies in patients with primary intracerebral haemorrhage found no benefit of gavestinel in this subgroup either.[3]

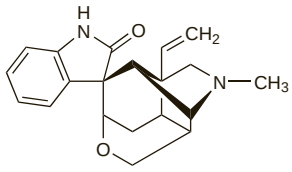
1. Lees KR, *et al.* Glycine antagonist (gavestinel) in neuroprotection (GAIN International) in patients with acute stroke: a randomised controlled trial. *Lancet* 2000; **355:** 1949–54.
2. Sacco RL, *et al.* Glycine antagonist in neuroprotection for patients with acute stroke: GAIN Americas: a randomized controlled trial. *JAMA* 2001; **285:** 1719–28.
3. Haley EC, *et al.* Gavestinel does not improve outcome after acute intracerebral hemorrhage: an analysis from the GAIN International and GAIN Americas studies. *Stroke* 2005; **36:** 1006–10.

Gelsemium

Gelsemium Root; Jessamine; Yellow Jasmine Root.

Корень Желтого Жасмина

CAS — 509-15-9 (gelsemine).



(gelsemine)

Profile

Gelsemium consists of the dried rhizome and roots of *Gelsemium sempervirens* (Loganiaceae). It contains toxic indole alkaloids including gelsemine ($C_{20}H_{22}N_2O_2$ = 322.4). It depresses the CNS and has been used mainly in neuralgic conditions, particularly trigeminal neuralgia and migraine.

Homoeopathy. Gelsemium has been used in homoeopathic medicines under the following names: Gelsemium sempervirens; Gels.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Fr.:*** Coquelusedal; Coquelusedal Paracetamol.

Gene Therapy

Terapéutica génica.

Генотерапия

Profile

Gene therapy is a product of the increasing knowledge of genetic function and the availability of methods to examine and manipulate the genome. Exogenous genetic material, which may be synthetic or recombinant nucleic acids (p.2355), is introduced into somatic cells (transfection) in such a way that the cells are able to express the products of the new genes. It may be used for therapeutic, prophylactic, or diagnostic purposes. Gene therapy should be distinguished from the use of products derived from organisms (usually micro-organisms) whose genome has been manipulated by similar recombinant DNA technology, for example the use of recombinant cytokines, monoclonal antibodies, or antisense products.

Gene therapy is under investigation in three main areas:

- the replacement of abnormal or defective genes in patients with inherited disease
- the alteration of the characteristics of cells to change their relative susceptibility to other therapies (for example by making haematopoietic stem cells more resistant to the adverse effects of antineoplastics, or by making tumour cells selectively express an enzyme that converts an otherwise non-toxic prodrug into a cytotoxic agent)
- for localised production of a biologically active substance that cannot be given directly or would have unacceptable effects if used systemically.

To date, all gene therapy in humans has been of differentiated somatic cells. Alteration of the human genome in a manner transmissible to offspring, either by treating the germ cells or the early embryo, is considered at present to pose insuperable ethical problems.

Various methods for delivery of genetic material have been investigated, none of which is yet completely satisfactory. These include biological vectors (e.g. viruses or plasmids) or stem cells that have been genetically modified, oncolytic viruses, nucleic acids, either naked plasmids or carried by delivery vehicles, and genetic vaccines. Antisense techniques to modify, correct, or silence aberrant genes are also being developed, as is RNA interference. Xenotransplantation of animal cells may also be an option. Removal of donor cells from the patient followed by *ex vivo* transfer of the new gene (by physical or viral methods) and return of the modified cells may be feasible for modifying haematopoietic stem cells. However, for most tissues, methods of *in vivo* transfer are required. Modified viruses rendered incapable of replicating have been widely studied as vectors for gene therapy. Retroviruses have the advantage that the DNA they carry is integrated into the host genome, resulting in permanent expression of the gene, but there has been some concern that they may disrupt existing genetic material with possibly oncogenic effect; in addition, their small size limits the size of gene that they can carry, and they are largely ineffective in infecting non-dividing cells. Adenoviruses are more stable and can infect non-dividing as well as dividing cells, but their genetic freight is not integrated into the chromosome and transmitted to the cell's progeny, and the gene products are therefore only expressed transiently; they are also highly immunogenic which limits repeated use. Some other viral types, including herpes simplex viruses, adeno-associated viruses, and lentiviruses, are also under investigation. Viruses with tropisms for a particular tissue may be useful in producing localised effects.

Chemical or physical methods for DNA delivery have been extensively investigated. Such methods include direct injection of DNA, the use of DNA complexes bound to a ligand which can be taken up by cells, formulation of DNA in liposomes which can fuse with cell membranes and allow the DNA to enter the cell, and more exotic methods such as 'gene guns', in which DNA-coated gold particles are fired into the cells. Although gene expression can be achieved after use of such methods, it is again transient because the new genetic material is not integrated with that of the host, and physical methods are currently less efficient and more limited in scope than viral ones.

Numerous clinical studies are being carried out. The first successful therapy was for severe combined immunodeficiency, a single-gene disorder due to deficiency of the enzyme adenosine deaminase. Transfection of the gene for this enzyme into the patient's T-cells *ex vivo* and re-infusion of the modified T-cells has been shown to produce substantial clinical improvement, although therapy must be repeated periodically because of the limited lifespan of the lymphocytes.

Studies in patients with cystic fibrosis have also shown some success, and a number of other single-gene disorders, including alpha$_1$ antitrypsin deficiency, familial hypercholesterolaemia, Gaucher disease, the haemoglobinopathies and haemophilias, and Duchenne muscular dystrophy are being studied or have been proposed as possible candidates.

Gene therapy is also under investigation in various acquired diseases, particularly in the management of various types of cancer. Strategies being studied include modification of tumour cells either to increase their immunogenicity or to render them selectively sensitive to antineoplastics, and transfection of tumour cells with tumour suppressor genes. Other disorders being studied clinically include HIV infection, rheumatoid arthritis, Parkinson's disease and atherosclerosis.

◊ Some reviews and references concerning gene therapy are listed below. See also under the discussions of individual diseases for comments on gene therapy in the context of their conventional treatment.

1. Hu WS, Pathak VK. Design of retroviral vectors and helper cells for gene therapy. *Pharmacol Rev* 2000; **52:** 493–511.
2. WHO. Gene transfer medicinal products. *WHO Drug Inf* 2002; **16:** 275–82.
3. Tomanin R, Scarpa M. Why do we need new gene therapy viral vectors? Characteristics, limitations and future perspectives of viral vector transduction. *Curr Gene Ther* 2004; **4:** 357–72.
4. Department of Health. Recommendations of the GTAC/CSM working party on retroviruses. Internet Document: May 2005. Available at: http://www.advisorybodies.doh.gov.uk/genetics/gtac/FinalrecommendationsJune2005.pdf (accessed 11/02/08)
5. Basu J, Willard HF. Artificial and engineered chromosomes: non-integrating vectors for gene therapy. *Trends Mol Med* 2005; **11:** 251–8.
6. Barzon L, *et al.* Versatility of gene therapy vectors through viruses. *Expert Opin Biol Ther* 2005; **5:** 639–62.
7. Sinn PL, *et al.* Gene therapy progress and prospects: development of improved lentiviral and retroviral vectors—design, biosafety, and production. *Gene Ther* 2005; **12:** 1089–98.
8. Wierdl M, Potter PM. Update on gene therapy approaches for cancer. *Curr Hematol Rep* 2005; **4:** 294–9.
9. Hart SL. Lipid carriers for gene therapy. *Curr Drug Deliv* 2005; **2:** 423–8.
10. Kaplan JM. Adenovirus-based cancer gene therapy. *Curr Gene Ther* 2005; **5:** 595–605.
11. Ohlfest JR, *et al.* Nonviral vectors for cancer gene therapy: prospects for integrating vectors and combination therapies. *Curr Gene Ther* 2005; **5:** 629–41.
12. Dobson J. Gene therapy progress and prospects: magnetic nanoparticle-based gene delivery. *Gene Ther* 2006; **13:** 283–7.
13. Pelletier R, *et al.* RNA based gene therapy for dominantly inherited diseases. *Curr Gene Ther* 2006; **6:** 131–46.
14. Park F, Gow KW. Gene therapy: future or flop. *Pediatr Clin North Am* 2006 **Aug:** 621–38.
15. Lavigne MD, Gorecki DC. Emerging vectors and targeting methods for nonviral gene therapy. *Expert Opin Emerg Drugs* 2006; **11:** 541–57.
16. Chan S, Harris J. The ethics of gene therapy. *Curr Opin Mol Ther* 2006; **8:** 377–83.
17. Cavazzana-Calvo M, Fischer A. Gene therapy for severe combined immunodeficiency: are we there yet? *J Clin Invest* 2007; **117:** 1456–65.

Gentian

Bitter Root; Enzianwurzel; Genciana; Gencijonų šaknys; Gentian Root; Gentiana; Gentianae radix; Gentianarot; Gentiane; Gentiane, racine de; Genziana; Hořcový kořen; Katkeronjuuri; Korzeń goryczki; Raiz de Genciana; Tárnicsgyökér.

Горький Корень

Pharmacopoeias. In *Eur.* (see p.vii), and *Jpn.*

Jpn includes Japanese Gentian, from *G. scabra* and other species.

Chin. also specifies *G. scabra* and other species.

Ph. Eur. 6.2 (Gentian Root; Gentian BP 2008). The dried, fragmented underground organs of *Gentiana lutea* yielding not less than 33% of water-soluble extractive. It has a characteristic odour. Protect from light.

Profile

Gentian is used as a bitter. An alcoholic infusion of gentian, bitter-orange peel, and lemon peel has been used as an ingredient in a number of bitter mixtures.

Homoeopathy. Gentian has been used in homoeopathic medicines under the following names: Gentiana lutea; Gent. lut.

Preparations

BP 2008: Acid Gentian Mixture; Alkaline Gentian Mixture; Compound Gentian Infusion; Concentrated Compound Gentian Infusion;
Ph. Eur.: Gentian Tincture.

Proprietary Preparations (details are given in Part 3)

Ger.: Digestivum-Hetterich S†; Enziagil Magenplus†; Sern-SL.

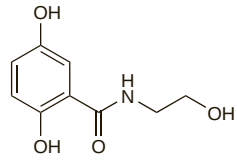
Multi-ingredient: ***Austral.:*** Calmo; Digest; Digestaid; Digestive Aid; Extralife Sleep-Care; Pacifenity†; Relaxaplex†; Sinulin†; ***Austria:*** Abdomilon N; Brady's-Magentropfen; China-Eisenwein; Mariazeller; Montana; Sigmann-Haustropfen; Sinupret; Solvopret; ***Braz.:*** Camomila; Digestar†; Estomafitino†; Gotas Digestivas; Xarope Iodo-Suma†; ***Canad.:*** Herbal Laxative; Herbal Laxative plus Yogurt; ***Cz.:*** Abdomilon†; Biotussil; Dr Theiss Schweden Krauter; Dr Theiss Schwedenbitter; Klosterfrau Melisana; Naturland Grosser Swedenbitter†; Original Schwedenbitter; Sinupret; ***Fr.:*** Elixir Grez†; Quintonine; ***Ger.:*** Abdomilon N; Amara-Pascoe; Amara-Tropfen; Anore X N†; Gallexier; Gastralon N†; Gastrol S†; Gastrosecur†; Hepaticum-Medice H†; Infi-tract†; Leber-Galle-Tropfen 83†; Majocarmin forte†; Majocarmin mite†; Montana N; Schwedentrunk Elixier; Sedovent; Sinupret; Stovalid N†; Unex Amarum†; ventri-loges N; ***Hong Kong:*** Sinupret; ***Hung.:*** Sinupret; ***Indon.:*** Sinupret; ***Ital.:*** Amaro Medicinale; Assenzio (Specie Composta)†; Caramelle alle Erbe Digestive; Centaurea (Specie Composta)†; Chinoidina†; Frerichs Maldifassi†; Genziana (Specie Composta)†; ***Mex.:*** Bisolsinus; ***Philipp.:*** Sinupret; ***Pol.:*** Dyspepsin; Kalms; Melisana Klosterfrau; Sinupret; ***Rus.:*** Herbion Drops for the Stomach (Гербион Желудочные Капли); Original Grosser Bittner Balsam (Оригинальный Большой Бальзам Биттнера); Sinupret (Синупрет); ***S.Afr.:*** Amara; Enzian Anaemodoron Drops; Helmontskruie; Lewensessens; Versterkdruppels; Wonderkroonessens; ***Singapore:*** Sinupret; ***Spain:*** Depurativo Richelet; ***Switz.:*** Demonatur Gouttes pour le foie et la bile; Gastrosan; Padma-Lax; Padmed Laxan; Sinupret; Strath Gouttes pour l'estomac; ***Thai.:*** Pepsitase; Sinupret; ***UK:*** Acidosis; Appetiser Mixture; Indigestion Mixture; Kalms; Quiet Tyme; Scullcap & Gentian Tablets; Stomach Mixture.

Gentisic Acid Ethanolamide

Etanolamida del ácido gentísico. 2,5-Dihydroxybenzoic acid ethanolamide.

$C_9H_{11}NO_4$ = 197.2.

CAS — 61969-53-7.



Profile

Gentisic acid ethanolamide has been used as a complexing agent in the manufacture of pharmaceutical preparations.

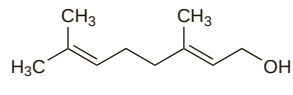
Geraniol

Lemonol. (*E*)-3,7-Dimethyl-2,6-octadien-1-ol; .

Гераниол

$C_{10}H_{18}O$ = 154.2.

CAS — 106-24-1.



Profile

Geraniol is a constituent of several essential oils and is used in insect repellent preparations. It was formerly used as an anthelmintic. Geraniol is also used as a flavour and in perfumery. Contact dermatitis has been reported.

◊ References.

1. Yamamoto A, *et al.* Contact urticaria from geraniol. *Contact Dermatitis* 2002; **46:** 52.