3. Piarroux R, *et al.* Are live saccharomyces yeasts harmful to patients? *Lancet* 1999; **353:** 1851–2.
4. Land MH, *et al.* Lactobacillus sepsis associated with probiotic therapy. *Pediatrics* 2005; **115:** 178–81.
5. Boyle RJ, *et al.* Probiotic use in clinical practice: what are the risks? *Am J Clin Nutr* 2006; **83:** 1256–64.
6. Hammerman C, *et al.* Safety of probiotics: comparison of two popular strains. *BMJ* 2006; **333:** 1006–8.

Composition and viability. Some preparations of probiotics have been found to contain smaller quantities or different species of organisms to those specified on the label.[1] An FAO/WHO working group[2] published some guidelines that should be followed in order to claim that a food has a probiotic effect. These include the genus, species, and strain of the organisms in the preparation to be stated on the product label using currently recognised systematic nomenclature, and a statement of the minimum number of viable organisms remaining at the end of the product shelf-life.

1. Hamilton-Miller JMT, *et al.* "Probiotic" remedies are not what they seem. *BMJ* 1996; **312:** 55–6.
2. FAO/WHO. *Guidelines for the evaluation of probiotics in food.* London Ontario, Canada: Food and Agriculture Organization of the United Nations, 2002. Also available at: http:// www.who.int/foodsafety/fs_management/en/probiotic_guidelines.pdf (accessed 11/02/08)

Uses. ***ALLERGIC DISORDERS.*** Oral ingestion of probiotic bacteria may play a role in the development of the adaptive immune system[1] and there has been some interest in their use in the management of allergic disorders such as atopic eczema.[2-5] However, reviews[6,7] of studies in allergic disorders have concluded that although there appears to be a reasonable theoretical basis for expecting benefit with probiotics, there are insufficient data to support their inclusion in routine treatment regimens for atopic eczema, perennial allergic rhinitis, or asthma.

1. Rinne M, *et al.* Effect of probiotics and breastfeeding on the *Bifidobacterium* and *Lactobacillus/Enterococcus* microbiota and humoral immune responses. *J Pediatr* 2005; **147:** 186–91.
2. Kalliomäki M, *et al.* Probiotics and prevention of atopic disease: 4-year follow-up of a randomised placebo-controlled trial. *Lancet* 2003; **361:** 1869–71.
3. Rosenfeldt V, *et al.* Effect of probiotics on gastrointestinal symptoms and small intestinal permeability in children with atopic dermatitis. *J Pediatr* 2004; **145:** 612–16.
4. Weston S, *et al.* Effects of probiotics on atopic dermatitis: a randomised controlled trial. *Arch Dis Child* 2005; **90:** 892–7.
5. Fölster-Holst R, *et al.* Prospective, randomized controlled trial on *Lactobacillus rhamnosus* in infants with moderate to severe atopic dermatitis. *Br J Dermatol* 2006; **155:** 1256–61.
6. Anonymous. Probiotics for atopic diseases. *Drug Ther Bull* 2005; **43:** 6–8.
7. Prescott SL, Björkstén B. Probiotics for the prevention or treatment of allergic diseases. *J Allergy Clin Immunol* 2007; **120:** 255–62.

GASTROINTESTINAL DISORDERS. Oral probiotics are under investigation for several gastrointestinal disorders and although they appear to be of benefit in some conditions, further study is required to confirm these findings. It is probable that efficacy depends on the species and strain of the organism as well as on the condition being treated.[1,2]

Conclusions from a systematic review[3] suggest that probiotics might be a useful adjunct to oral rehydration therapy in the treatment of acute infectious *diarrhoea* in adults and children. A meta-analysis[4] of studies of *Lactobacillus* therapy in children reached a similar conclusion. However, it was not possible to draw up definitive treatment guidelines because of a lack of standardisation in probiotic regimens, patient groups, or definition of acute diarrhoea between the available studies.[3,4] Meta-analyses[5,6] and a systematic review[7] of studies investigating the use of probiotics in the prevention of antibiotic-associated diarrhoea in adults[5] and children[5-7] also suggest a beneficial effect, although again, further clinical confirmation is required before they can be routinely recommended.[5-7] A review[8] of studies that looked specifically at treatment or prevention of *Clostridium difficile*-associated diarrhoea with the probiotics *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii* concluded that while these specific probiotics might be useful in patients at risk of recurrent *C. difficile* infection, the potential risks of bacteraemia or fungaemia in this particular patient group might outweigh any benefit.

Probiotics have been investigated to correct aberrant intestinal microflora associated with chronic *inflammatory bowel disease* and reviews of such studies suggest some benefit in the prevention and treatment of ulcerative colitis[9-11] and maintenance of remission in pouchitis,[10-12] although the data are not so clear for Crohn's disease.[10,13] Larger controlled clinical studies, again with standardised probiotic preparations and treatment regimens, are necessary to establish the place of probiotics in the management of inflammatory bowel disease.[9-13] Probiotics do not appear to improve abdominal pain in patients with *irritable bowel syndrome* but they may reduce bloating.[14]

Probiotics given to preterm neonates of very low birth-weight reduced the incidence and severity of *necrotising enterocolitis* in 2 randomised controlled studies.[15,16] A systematic review[17] of these and other controlled studies reached the same conclusion, although the authors called for confirmation of these results by a larger study to strengthen the case for routine use of probiotics in preterm neonates.

Probiotics have also been tried in constipation[18] and infantile colic.[19]

1. Anonymous. Probiotics for gastrointestinal disorders. *Drug Ther Bull* 2004; **42:** 85–8.
2. Limdi JK, *et al.* Do probiotics have a therapeutic role in gastroenterology? *World J Gastroenterol* 2006; **12:** 5447–57.
3. Allen SJ, *et al.* Probiotics for treating infectious diarrhoea. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2003 (accessed 11/02/08).
4. Van Niel CW, *et al. Lactobacillus* therapy for acute infectious diarrhea in children: a meta-analysis. *Pediatrics* 2002; **109:** 678–84.
5. D'Souza AL, *et al.* Probiotics in prevention of antibiotic associated diarrhoea: meta-analysis. *BMJ* 2002; **324:** 1361–6.
6. Szajewska H, *et al.* Probiotics in the prevention of antibiotic-associated diarrhea in children: a meta-analysis of randomized controlled trials. *J Pediatr* 2006; **149:** 367–72.
7. Johnston BC, *et al.* Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2007 (accessed 11/02/08).
8. Segarra-Newnham M. Probiotics for *Clostridium difficile*-associated diarrhea: focus on *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*. *Ann Pharmacother* 2007; **41:** 1212–21.
9. Bai A-P, Ouyang Q. Probiotics and inflammatory bowel diseases. *Postgrad Med J* 2006; **82:** 376–82.
10. Ewaschuk JB, Dieleman LA. Probiotics and prebiotics in chronic inflammatory bowel diseases. *World J Gastroenterol* 2006; **12:** 5941–50.
11. Chapman TM, *et al.* VSL#3 probiotic mixture: a review of its use in chronic inflammatory bowel diseases. *Drugs* 2006; **66:** 1371–87.
12. Sandborn W, *et al.* Pharmacotherapy for induction and maintenance of remission in pouchitis. Available in the Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 1998 (accessed 11/02/08).
13. Rolfe VE, *et al.* Probiotics for maintenance of remission in Crohn's disease. Available in the Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 11/02/08).
14. Bausserman M, Michail S. The use of *Lactobacillus* GG in irritable bowel syndrome in children: a double-blind randomized control trial. *J Pediatr* 2005; **147:** 197–201.
15. Bin-Nun A, *et al.* Oral probiotics prevent necrotizing enterocolitis in very low birth weight neonates. *J Pediatr* 2005; **147:** 192–6.
16. Lin H-C, *et al.* Oral probiotics reduce the incidence and severity of necrotizing enterocolitis in very low birth weight infants. *Pediatrics* 2005; **115:** 1–4.
17. Deshpande G, *et al.* Probiotics for prevention of necrotising enterocolitis in preterm neonates with very low birthweight: a systematic review of randomised controlled trials. *Lancet* 2007; **369:** 1614–20.
18. Banaszkiewicz A, Szajewska H. Ineffectiveness of *Lactobacillus* GG as an adjunct to lactulose for the treatment of constipation in children: a double-blind, placebo-controlled randomized trial. *J Pediatr* 2005; **146:** 364–9.
19. Savino F, *et al. Lactobacillus reuteri* (American Type Culture Collection Strain 55730) versus simethicone in the treatment of infantile colic: a prospective randomized study. *Pediatrics* 2007; **119:** e124-e30. Available at: http:// pediatrics.aappublications.org/cgi/reprint/119/1/e124 (accessed 11/02/08)

UROGENITAL INFECTIONS. Probiotic preparations given orally or intravaginally are under investigation for the prevention or treatment of vaginal infections. Reviews of studies in vulvovaginal candidiasis[1] and bacterial vaginosis[2] concluded that while there was some indication of benefit, larger controlled studies are required to confirm efficacy and the place of probiotics in therapy. A systematic review[3] confirmed that probiotics may be of benefit in the prevention and treatment of bacterial vaginosis in pregnancy but due to insufficient data it was not possible to assess the effect that this might have in preventing preterm labour. A review[4] of studies investigating probiotics for the prevention of urinary-tract infections in women has suggested some benefit.

1. Falagas ME, *et al.* Probiotics for prevention of recurrent vulvovaginal candidiasis: a review. *J Antimicrob Chemother* 2006; **58:** 266–72.
2. Falagas ME, *et al.* Probiotics for the treatment of women with bacterial vaginosis. *Clin Microbiol Infect* 2007; **13:** 657–64.
3. Othman M, *et al.* Probiotics for preventing preterm labour. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 11/02/08).
4. Falagas ME, *et al.* Probiotics for prevention of recurrent urinary tract infections in women: a review of the evidence from microbiological and clinical studies. *Drugs* 2006; **66:** 1253–61.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Acidofilofago; Flevic; Floratil; Lactinex; Tropivag; ***Austral.:*** Bioglan Acidophilus; Bioglan Superdophilus; Forbiotic; ProTract; ***Austria:*** Antibiophilus; Bioflorin; Lactofit; Reflor; Symbioflor Enterococcus; Yomogi; ***Belg.:*** Enterol; Lacteol; ***Braz.:*** Flomicin; Floratil; Floren; Florent; Lactipan; Leiba; Repoflor; ***Canad.:*** Bacid; Lacidofil; ***Chile:*** Bio-Flora; Biolactus; Econormotil; Gastrofloral; Lacteol Forte†; Lactil; Perenteryl; Perocur†; ***Cz.:*** Enterol; Santax S†; Solco-Trichovac†; ***Denm.:*** Paraghurt; Precosa; ***Fin.:*** Lactophilus; Precosa; ***Fr.:*** Bacilor; Bioprotus; Diarlac†; Gynophilus; Lacteol; Lyo-Bifidus; Ultra-Levure; Ultraderme†; ***Ger.:*** Acidophilus†; Hylak N; Hylak Plus; Infectodiarrstop GG†; Lacteol; Lyseen; Omnisept†; Paidoflor; Perenterol; Symbioflor 1; Vagiflor; ***Gr.:*** Ultra-Levure; ***Hong Kong:*** Bioflor; Lacteol; Reuteri; ***Hung.:*** Enterol; Gynevac; Symbioflor 1; ***India:*** Cefocef-LB; Myconip; Sporlac; ***Indon.:*** Lacbon; Rillus; ***Ital.:*** Bioflorin; Calagin; Codex; Dicoflor; Ecoflorina; Ferlactis†; Inulac; Lab/A†; Lacteol; Lactonorm; Ramno-Flor†; Regolact Plus; Reuflor; ***Mex.:*** Floratil; Lacteol Fort; Lactipan; Lactocil; Lactovita; Lioactil; Neoflor; Sinuberase; ***NZ:*** Blis K12 Throat Guard; ***Philipp.:*** Infloran; ***Pol.:*** Enterol; Lactovaginal; Lakcid†; ***Port.:*** Antibiophilus; Enterol†; Lacteol; UL 250†; ***Rus.:*** Enterol (Энтерол); Gastropharm (Гастрофарм); IRS 19 (ИРС 19); ***S.Afr.:*** Actiflora; Inteflora; ***Singapore:*** DiarrStope; Lacteol; Protexin; Reutefene; ***Spain:*** Casenfilus; Lacteol; Lactofilus; Ultra-Levura; ***Swed.:*** Precosa; ***Switz.:*** Bioflorin; Fiormil†; Florosan; Lacteol†; Lactoferment; Perenterol; SolcoTrichovac Lyophilisat; Ultra-Levure; Ventrux†; ***Thai.:*** Lacbon†; Lacteol†; ***Turk.:*** Reflor; ***UK:*** Bio Acidophilus; Biodophilus; Gum PerioBalance; Infacol Probiotic; ***USA:*** Acidophilus; Bacid; Florastor; Intestinex; Kala; Lactinex; Lacto-Key; MoreDophilus; Pro-Bionate; Superdophilus; ***Venez.:*** Florcidin; Florestor; Lacteol; Lactobacilos; Liolactil; Proflor.

Multi-ingredient: ***Arg.:*** Bioflora; Biol Preo; Factor Bioenterico; Faelac†; Nilflux; Totalflora; Tropivag Plus; ***Austral.:*** Acidophilus Bifidus; Acidophilus Plus; Cyto-Bifidus; ***Austria:*** Gynoflor; Hylak; Hylak Forte; Infloran; Omniflora; Prosymbioflor†; Trevis; ***Belg.:*** Carbolactanose; Gynoflor; ***Canad.:*** Fermalac Vaginal; ***Chile:*** Bion 3; ***Cz.:*** Fermalac Vaginal; Gynoflor; Hylak Forte; Imudon; IRS 19†; Lacidofil; Solco-Urovac†; ***Fr.:*** Actyfilus; Biolactyl; Biotravel; Ergyphilus; Estrofort; Florgynal; Imgalt; Imudon†; IRS 19†; Maxi-Flore; Ophidus; Probionat; Triphidus; Trophigil; Ultrabiotique; ***Ger.:*** Antiprurit†; Gynoflor; InfectoDiarrstop LGG; IRS 19; Omniflora N; Perison; Pro-Symbioflor; StroVac; ***Hong Kong:*** Infloran; Lacspan; Protexin Balance; Protexin Balance+; Protexin Restore; Protexin Vitality; Shin-Biofermin S; ***Hung.:*** Gynoflor; Trevis; ***India:*** ABClox; Ampilox-LB; Amplus; Ampoxin-LB; Bicidal Plus; Bifilac; Biomoxil-LB; Campicillin Plus; Cefix LB; Cephadex LB; Clax; Imox-Clo LB; Lactisyn; LMX; Megaclox LB; Novaclox LB; Novamox LB; Nutrolin-B; Symbiotik; Symoxyl-LB; Vitazyme; Vizylac; ***Indon.:*** Dialac; Gastro-Ad; Lacidofil; Lacto-B; Laktobion; Protexin; Synbio; ***Ital.:*** Al-Flor†; Altaflora Probiotici; Bifilact; Bio Fibralax Bi-Attivo; Bio Flora; Biolactine; Colifagina; Decon Lavanda; Ecofermenti; Endolac; Enterolactis; Enteroseven; Fermenturto-Lio; Floragermina 6; Florbiox†; Florelax; Floren; Floridral; Florvis GG; Gastroenterol; Genefilus F19; Giflorex; Ginil; Infloran; Infloran Bio; Kiri; Lactipan; Lactisporin; Lactivis; Lactogermine; Lactolife; Liozim; Liverton; Neo Lactoflorene; Neogyn; Nepiros; Ninfagin; Psyllogel Fermenti; Ramno Fix; Ramnoflor Plus; Rivuclin; Triacid; Vaxitiol; Yovis; Yovita; ***Jpn:*** The Guard Seichojo; ***Malaysia:*** Hexbio; ***Mex.:*** Neo-Panlacticos; Neo-Panlacticos Plus; Pro-T-Flor; ***Pol.:*** IRS 19; Lacidofil; Trilac; ***Port.:*** Coli-Fagina S; Gynoflor; Infloran†; ***Rus.:*** Acipol (Аципол); Bifiform (Бифиформ); Hylak Forte (Хилак Форте); Imudon (Имудон); Linex (Линекс); SolcoTrichovac (Солкотриховак); ***S.Afr.:*** Culturelle; Culturelle VC; ***Spain:*** Infloran; ***Switz.:*** Gynoflor; Infloran; Ribolac; SolcoTrichovac; ***Thai.:*** Infloran; ***Turk.:*** Gynoflor; ***UK:*** Acidophilus Plus; Beneflora; Culture Care; Fibre Dophilus; Natudophilus; Vinalac; ***USA:*** Acidophilus with Bifidus; Floranex; Pamine FQ Kit; SynBiotics-3; VSL#3; ***Venez.:*** Glutapak-R.

Promelase *(pINN)*

Promelasa; Promélase; Promelasum; Seaprose S.

Промелаза

CAS — 9074-07-1.

Profile

Promelase is an alkaline protease derived from *Aspergillus melleus*. It has been taken by mouth in doses of 30 to 90 mg daily for its supposed benefit in oedema and inflammation associated with trauma, infection, and surgical procedures.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Altan; Flaminase; Mezen†; ***Port.:*** Onoprose†; ***Thai.:*** Korynase†.

Pronase

Profile

Pronase is a mixture of proteinases obtained from *Streptomyces griseus*.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Empynase.

Propolis

Bee Glue; Propóleo; Própolis.

Прополис

Profile

Propolis is a resinous substance collected by bees, primarily, at least in temperate climates, from poplar buds (see also p.2371) and to a lesser extent from conifers. It is mixed with wax by bees and used in the construction and maintenance of their hives. Propolis is composed of resins, balsams, essential and aromatic oils, and pollen, although the exact proportions of each varies from region to region, bee species, and local flora, therefore making standardisation of propolis for medicinal use difficult. Propolis has been reported to have anti-inflammatory and antimicrobial properties. It has been used as a nutritional supplement and in preparations for coughs, mouth disorders, and skin disorders. It has been used as an ointment for the relief of symptoms of herpes labialis. Propolis has also been used in cosmetics and varnishes.

Hypersensitivity reactions have been reported.

◊ For reference to hypersensitivity reactions with bee products, including propolis, see under Royal Jelly, p.2382.

Further references to propolis are given below.

1. Grange JM, Davey RW. Antibacterial properties of propolis (bee glue). *J R Soc Med* 1990; **83:** 159–60.
2. Krol W, *et al.* Synergistic effect of ethanolic extract of propolis and antibiotics on the growth of Staphylococcus aureus. *Arzneimittelforschung* 1993; **43:** 607–9.
3. Volpert R, Elstner EF. Interactions of different extracts of propolis with leukocytes and leukocytic enzymes. *Arzneimittelforschung* 1996; **46:** 47–51.
4. Murray MC, *et al.* A study to investigate the effect of a propolis-containing mouthrinse on the inhibition of de novo plaque formation. *J Clin Periodontol* 1997; **24:** 796–8.