both drugs can be given for an equivalent effect for each individual drug, so reducing side-effects and drug burden.

Therefore, the present invention is an agent comprising theobromine and an expectorant, or an agent comprising theobromine and a mucolytic.

In one embodiment, there is provided an agent consisting of theobromine and an expectorant, or theobromine and a mucolytic, or theobromine, an expectorant and a mucolytic as a combined preparation, wherein the agent is formulated for simultaneous administration of the theobromine with the expectorant; or wherein the agent is formulated for simultaneous administration of the theobromine with the mucolytic; or wherein the agent is formulated for simultaneous administration of the theobromine with the expectorant and the mucolytic.

In one embodiment there is provided a pharmaceutical composition comprising an agent as defined above and one or more excipients.

In one embodiment, there is provided the use of an agent as defined above or a pharmaceutical composition as defined above for the manufacture of a medicament for treating cough.

Description of the Figures

Figure 1 shows the total number of coughs in guinea-pigs during a 10 minute exposure and 5 minute recovery period to citric acid (1M), following pre-treatment with either vehicle (p.o.), theobromine (10 mg kg^{-1}, i.p), guaifenesin (30 mg/kg, p.o.) or theobromine (10 mg/kg, p.o.) combined with guaifenesin (30 mg/kg. p.o.). Each column represents the mean and the vertical bars the s.e. mean. Changes in total cough number in the presence of theobromine, guaifenesin and theobromine in combination with guaifenesin were compared to vehicle dosed animals using ANOVA followed by Dunnetts test to compare the means. **P<0.01, *P<0.05.

Description of the Invention

Any suitable form of theobromine can be chosen. These include salts, prodrugs and active metabolites. The additional agent (expectorant or mucolytic) may be used in an amount that is already known for its use, although combination according to this invention means that a reduced dose may be effective. A combination according to the invention may be provided in a single

formulation or in separate formulations, for combined, simultaneous or sequential administration.

Expectorants suitable for use in the invention are ambroxol, ammonium bicarbonate, ammonium carbonate, bromhexine, calcium iodide, carbocysteine, guaiacol, guaicacol benzoate, guaiacol carbonate, guaiacol phosphate, guaifenesin, guaithylline, hydriodic acid, iodinated glycerol, potassium guaiacolsulfonate, potassium iodide, sodium citrate, sodium iodide, storax terebene, terpin, trifolium, Althea root, Antimony pentasulfide, Creosote, Ipecacuanha (Syrup of ipecac), levoverbenone, Senega and Tyloxapol. Preferably, the expectorant is guaifenesin.

Mucolytic agents suitable for use in the invention are acetylcysteine, bromhexine, carbocysteine, domiodol, erdostine, letostine, lysozyme, mecysteine hydrochloride, mesna, sobrerol, stepronin, tiopronin, tyloxapol,

CLAIMS

1. An agent consisting of theobromine and an expectorant, or theobromine and a mucolytic, or theobromine, an expectorant and a mucolytic as a combined preparation, wherein the agent is formulated for simultaneous administration of the theobromine with the expectorant; or wherein the agent is formulated for simultaneous administration of the theobromine with the mucolytic; or wherein the agent is formulated for simultaneous administration of the theobromine with the expectorant and the mucolytic.

2. An agent consisting of theobromine and an expectorant, or theobromine and a mucolytic, or theobromine, an expectorant and a mucolytic as a combined admixture preparation.

3. An agent according to claim 1, consisting of theobromine, an expectorant and a mucolytic, wherein the agent is formulated for simultaneous administration of the theobromine with the expectorant and the mucolytic.

4. An agent according to claim 2, consisting of theobromine, an expectorant and a mucolytic as a combined admixture preparation.

5. The agent according to any one of claims 1-4, wherein the expectorant is ambroxol, ammonium bicarbonate, ammonium carbonate, bromhexine, calcium iodide, carbocysteine, guaiacol, guaiacol benzoate, guaiacol carbonate, guaiacol phosphate, guaifenesin, guaithylline, hydriodic acid, iodinated glycerol, potassium guaiacolsulfonate, potassium iodide, sodium citrate, sodium iodide, storax, terebene, terpin, trifolium, Althea root, antimony pentasulfide, creosote, ipecacuanha, ievoverbenone, senega or tyloxapol.

6. The agent according to any one of claims 1-5, wherein the mucolytic is acetylcysteine, bromhexine, carbocysteine, domiodol, erdostine, letostine, lysozyme, mecysteine hydrochloride, mesna, sobrerol, stepronin, tiopronin, tyloxapol, ambroxol, ammonium chloride, dornase alfa, eprazinone, erdosteine, letosteine or neltenexine.

7. The agent according to any one of claims 1-6, wherein the theobromine is an amount of between 1 and 3000 mg.

8. The agent according to claim 7, wherein the theobromine is in an amount of between 50 and 1500 mg.

9. The agent according to claim 8, wherein the theobromine is in an amount of between 400 mg to 1000 mg.

10. The agent according to anyone of claims 1-9 manufactured for oral administration.

11. The agent according to anyone of claims 1-10 characterized by being prepared as a tablet, capsule, troche, lozenge, powder, granule, suspension, syrup or emulsion.

12. A pharmaceutical composition comprising an agent as defined in any one of claims 1-9 and one or more excipients.

13. The composition according to claim 12, further comprising one or more of sweetening agents, flavoring agents, coloring agents and/or preserving agents.

14. The composition according to claim 12 or claim 13, wherein the composition is manufactured for oral administration.

15. The composition according to any one of claims 12-14, wherein the composition is prepared as a tablet, capsule, troche, lozenge, powder, granule, suspension, syrup or emulsion

16. Use of an agent as defined in any one of claims 1-11 or a pharmaceutical composition as defined in any one of claims 12-15 for the manufacture of a medicament for treating cough.

CLAIMS

1. An agent comprising theobromine and an expectorant, or an agent comprising theobromine and a mucolytic.

2. An agent according to claim 1, comprising theobromine, an expectorant and a mucolytic.

3. An agent according to claim 1 or claim 2, as a combined preparation for simultaneous, sequential or separate use in therapy.

4. An agent according to any preceding claim, wherein the therapy is of a cough.

5. An agent according to any preceding claim, wherein the agent is administered via the oral, inhaled, topical, sublingual, intranasal, intravenous, rectal or vaginal routes.

6. An agent according to claim 1, comprising theobromine and an expectorant.

7. An agent according to claim 6, wherein the expectorant is ambroxol, ammonium bicarbonate, ammonium carbonate, bromhexine, calcium iodide, carbocysteine, guaiacol, guaicacol benzoate, guaiacol carbonate, guaiacol phosphate, guaifenesin, guaithylline, hydriodic acid, iodinated glycerol, potassium guaiacolsulfonate, potassium iodide, sodium citrate, sodium iodide, storax terebene, terpin, trifolium, Althea root, Antimony pentasulfide, Creosote, Ipecacuanha (Syrup of ipecac), levoverbenone, Senega or Tyloxapol.

8. An agent according to any of claims 1 to 5, comprising theobromine and a mucolytic.

9. An agent according to claim 8, wherein the mucolytic is acetylcysteine, bromhexine, carbocysteine, domiodol, erdostine, letostine, lysozyme, mecysteine hydrochloride, mesna, sobrerol, stepronin, tiopronin, tyloxapol, ambroxol, ammonium chloride, Dornase alfa, Eprazinone, Erdosteine, Letosteine or Neltenexine.

10. An agent according to any preceding claim, wherein the theobromine is to be dosed daily, in a dose of between 1 and 3000 mg, preferably between 50 and 1500 mg, even more preferably, between 400 mg to 1000 mg.