1:5 1:6, 1.7, 1.8, 1.9 or 2.0. In some embodiments, the ratio of cyclobenzaprine (2.4 mg, MW 275.387) to K_2HPO_4 (1.05 mg, MW 174.2) is 0.69.

Cyclobenzaprine and amitriptyline metabolism

[0092] Cyclobenzaprine rapidly distributes out of the vasculature after intravenous (IV) bolus administration in humans (Hucker et al., J Clin Pharmacol 17:719-727 (1977), Hucker et al., Drug Metab Dispos 6:659-672 (1978), Till at al., Annu Rev Pharmacol Toxicol 40:581-616 (2000), and Winchell et al., J Clin Pharmacol 42:61-69 (2002)). The amount of cyclobenzaprine in plasma within 3 to 30 minutes was less than 5% of the theoretical initial concentration (C_{init}) of each infused dose, and a 3 minute time point resulted in a relatively higher C_{init}. Together, this information shows that cyclobenzaprine is rapidly partitioned out of plasma. Since greater than 95% of injected cyclobenzaprine is cleared from plasma before the first time point of any of the four studies listed above, they are not informative about the half-life of the first phase of IV cyclobenzaprine distributing out of plasma, beyond establishing that an upper limit for the half-life of the first phase is clearly less than 3-5 minutes.

[0093] Amitriptyline is structurally related to cyclobenzaprine and differs from cyclobenzaprine chemically by lacking the C10-C11 double-bond in the central cycloheptyl ring. However, changes in chemical structure can affect drug actions on normal or pathological tissues as well as absorption, disposition, metabolism and excretion. Amitriptyline and its desmethyl metabolite nortriptyline are the active pharmaceutical ingredients of the tricyclic anti-depressants (TCAs) Elavil® and Pamelor®, respectively. Amitriptyline, like cyclobenzaprine, is rapidly partitioned out of plasma. The pharmacokinetics of IV administration of cyclobenzaprine or amitriptyline or IV administration of amitriptyline can be described by a two-compartment model containing a plasma "central" compartment and a "peripheral" compartment.

[0094] Neither cyclobenzaprine nor amitriptyline is an effective long-term treatment for fibromyalgia in any formulation that has been tested, for example currently available formulations were not effective over six months of treatment

CLAIMS

1. A composition for transmucosal absorption comprising a pharmaceutically acceptable cyclobenzaprine salt and a basifying agent, wherein the composition comprises less than 9 mg of the cyclobenzaprine salt, and wherein the molar ratio of cyclobenzaprine to basifying agent in the composition is between 1:0.69 to 1:6.

2. The composition of claim 1, wherein the composition comprises 0.1 mg to 5 mg of the pharmaceutically acceptable cyclobenzaprine salt.

3. The composition of claim 1, wherein the pharmaceutically acceptable cyclobenzaprine salt is cyclobenzaprine HCl and the amount of cyclobenzaprine in the composition is less than or equal to 2.4 mg.

4. The composition of claim 1, wherein the pharmaceutically acceptable cyclobenzaprine salt is cyclobenzaprine HCl and the amount of cyclobenzaprine in the composition is less than or equal to 4.8 mg.

5. The composition of claim 1, wherein the pharmaceutically acceptable cyclobenzaprine salt is cyclobenzaprine HCl and is present in an amount of 2.8 mg.

6. The composition of claim 1, wherein the pharmaceutically acceptable cyclobenzaprine salt is cyclobenzaprine HCl and is present in an amount of 5.6 mg.

7. The composition of any one of claims 1-6, wherein the basifying agent is selected from the group consisting of potassium dihydrogen phosphate, dipotassium hydrogen phosphate, tripotassium phosphate, sodium carbonate, sodium bicarbonate, calcium carbonate, calcium bicarbonate, TRIS buffer, sodium dihydrogen phosphate, disodium hydrogen phosphate, trisodium phosphate, potassium carbonate, potassium bicarbonate, potassium acetate, sodium acetate, dipotassium citrate, tripotassium citrate, disodium citrate and trisodium citrate.

8. The composition of any one of claims 1-7, wherein the transmucosal absorption is oral absorption.

9. The composition of claim 8, wherein the oral absorption is sublingual absorption.

10. The composition of claim 9, wherein the composition is selected from the group consisting of a sublingual tablet, a sublingual film, a sublingual powder, and a sublingual spray solution.

11. The composition of any one of claims 1-8, wherein the transmucosal absorption is buccal absorption.

12. The composition of claim 11, wherein the composition is selected from the group consisting of a buccal tablet, a lozenge, a buccal powder, and a buccal spray solution.

13. The composition of any one of claims 1-7, wherein the transmucosal absorption is intranasal absorption.

14. The composition of claim 13, wherein the composition is a nasal spray solution.

15. The composition of any one of claims 1-7, wherein the transmucosal absorption is pulmonary absorption.

16. The composition of claim 15, wherein the composition is selected from the group consisting of an aerosolized composition and an inhalable dry powder.

17. Use of a composition of any one of claims 1-7 in the manufacture of a medicament for transmucosal absorption for treating a disease or condition in an individual in need thereof, wherein the disease or condition is post-traumatic stress disorder (PTSD), fibromyalgia, depression, traumatic brain injury, sleep disorder, non-restorative sleep, chronic pain, muscle spasm, or anxiety disorder.

18. The use of claim 17, wherein the disease or condition is post-traumatic stress disorder (PTSD).

19. The use of claim 18, wherein the disease or condition is the development, initiation, consolidation, or perpetuation of PTSD following a traumatic event.

20. The use of any one of claims 17-19, wherein the transmucosal absorption is sublingual absorption.

21. The use of claim 20, wherein the medicament is selected from the group consisting of a sublingual tablet, a sublingual film, a sublingual powder, and a sublingual spray solution.

22. The use of any one of claims 17-19, wherein the transmucosal absorption is buccal absorption.

23. The use of claim 22, wherein the medicament is selected from the group consisting of a buccal tablet, a lozenge, a buccal powder, and a buccal spray solution.

24. The use of any one of claims 17-19, wherein the transmucosal absorption is intranasal absorption.

25. The use of claim 24, wherein the medicament is a nasal spray solution.

26. The use of any one of claims 17-19, wherein the transmucosal absorption is pulmonary absorption.

27. The use of claim 26, wherein the medicament is selected from the group consisting of an aerosolized composition and an inhalable dry powder.