CLAIMS

1. A method of enhancing the oral bioavailability of zoledronic acid comprising orally administering a dosage form containing zoledronic acid in the disodium salt form.

2. The method of claim 1, wherein the zoledronic acid in the disodium salt form provides an enhancement to bioavailability, as compared to zoledronic acid in the diacid form, which adds to any enhancement to bioavailability provided by any bioavailability-enhancing agents in the dosage form.

3. The method of claim 1, wherein the zoledronic acid in the disodium salt form is administered to a mammal in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 4 ng•h/mL to about 2000 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

4. The method of claim 1, wherein the zoledronic acid in the disodium salt form is administered at an interval of about 3 to about 4 weeks in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 100 ng•h/mL to about 2000 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

5. The method of claim 1, wherein the zoledronic acid in the disodium salt form is administered weekly, or 3 to 5 times in a month, in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 20 ng•h/mL to about 700 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

6. The method of claim 1, wherein the zoledronic acid in the disodium salt form is administered daily in an amount that provides an area under the plasma concentration curve of zoledronic acid of about 4 ng•h/mL to about 100 ng•h/mL to the mammal each time the zoledronic acid in the disodium salt form is administered.

7. The method of claim 1, wherein the dosage form is a solid.

8. The method of claim 1, wherein the bioavailability of zoledronic acid is improved by at least about 20% as compared to administration of zoledronic acid in the diacid form.

9. The method of claim 1, further comprising administering, on a molar basis, less of the zoledronic acid in the disodium salt form than would be administered of zoledronic acid in the diacid form in order to achieve the same plasma levels of zoledronic acid.

10. The method of claim 9, wherein at least about 10 mole% less of the disodium salt form is administered as compared to the amount of zoledronic acid in the diacid form that would be administered in order to achieve the same plasma levels of zoledronic acid.

11. The method of claim 9, wherein the disodium salt form is administered in an amount, on a molar basis, that has a value of about $0.8n_d$ to about $1.2n_d$, wherein:

$$n_d = (b_a/b_d)(n_a)$$

wherein b_a is the bioavailability of the diacid form, b_d is the bioavailability of the disodium salt form, and n_a is the number of moles of zoledronic acid in the diacid form that would be administered in order to achieve the same plasma levels of zoledronic acid.

12. The method of claim 1, wherein the zoledronic acid is used to treat an inflammatory condition.

13. The method of claim 1, wherein the zoledronic acid is used to treat arthritis or complex regional pain syndrome.

14. The method of claim 1, wherein the zoledronic acid is for the treatment of an inflammatory condition, arthritis, or complex regional pain syndrome, and wherein:

a first oral dosage form is administered; and

a second oral dosage form is administered;

wherein, with respect to the first oral dosage form, the second oral dosage form is administered at 10 x T_{max} or greater, wherein T_{max} is the time of maximum plasma concentration for the first oral dosage form.

15. An oral dosage form comprising zoledronic acid in the disodium salt form, wherein the bioavailability, in a mammal, of zoledronic acid in the disodium salt form is greater than the bioavailability of zoledronic acid in the diacid form would be in the same dosage form.

16. The oral dosage form of claim 15, wherein the dosage form contains an amount of zoledronic acid in the disodium salt form that provides an area under the plasma concentration curve of zoledronic acid of about 100 ng•h/mL to about 2000 ng•h/mL to a human being to which the dosage form is administered.

17. The oral dosage form of claim 15, wherein the dosage form contains an amount of zoledronic acid in the disodium salt form that provides an area under the plasma concentration curve of zoledronic acid of about 20 ng•h/mL to about 700 ng•h/mL to a human being to which the dosage form is administered.

18. The oral dosage form of claim 15, wherein the dosage form contains an amount of zoledronic acid in the disodium salt form that provides an area under the plasma concentration curve of zoledronic acid of about 4 ng•h/mL to about 100 ng•h/mL to a human being to which the dosage form is administered.

19. The oral dosage form of claim 15, wherein the disodium salt form is present in a lower molar amount than would be present if the zoledronic acid were in the diacid form; and wherein the zoledronic acid in the disodium salt form has an improved bioavailability as compared to the zoledronic acid in the diacid form to the extent that the lower molar amount of the disodium salt in the dosage form does not reduce the amount of zoledronic acid delivered to the plasma of a mammal.

20. The oral dosage form of claim 185, containing at least about 20 mole% less of the disodium salt form as compared to the amount of the zoledronic acid in the diacid form that would be present if the zoledronic acid were in the diacid form.

21. The oral dosage form of claim 185, wherein the disodium salt form is present in an amount, on a molar basis, that has a value of about $0.9n_d$ to about $1.1n_d$, wherein:

$$n_d = (b_a/b_d)(n_a)$$

wherein b_a is the bioavailability of the diacid form, b_d is the bioavailability of the disodium salt form, and n_a is the number of moles of the diacid form that would be present if the zoledronic acid were in the diacid form.

22. The oral dosage form of claim 21, wherein the disodium salt is administered in an amount that has a value of about n_d.

23. The oral dosage form of claim 15, wherein the dosage form is a solid.

24. The oral dosage form of claim 15, wherein the bioavailability of zoledronic acid in the disodium salt form is improved by at least about 10% as compared to an otherwise identical dosage form containing zoledronic acid in the diacid form.

25. The method of claim 1, wherein the zoledronic acid is for the treatment of an inflammatory condition, arthritis, or complex regional pain syndrome, and wherein:

only a single oral dosage form is administered; or

a first oral dosage form is administered, and a second oral dosage form is administered after the first oral dosage form;

wherein the second oral dosage form is administered before the maximum pain relieving effect of the first oral dosage form is achieved, or the second oral dosage form is administered before an observable pain relieving effect is achieved.

26. The method of claim 25 wherein the second oral dosage form is administered before an observable pain relieving effect is achieved.

27. The method of claim 1, wherein the zoledronic acid is for the treatment of an inflammatory condition, arthritis, or complex regional pain syndrome, and

wherein a first oral dosage form is administered, followed by administration of a second oral dosage form;

wherein the second oral dosage form is administered after the maximum pain relieving effect of the first oral dosage form is achieved; and

the second oral dosage form is administered while a pain relieving effect from the first oral dosage form is observable.

28. The method of claim 25, wherein the second oral dosage form is administered about 24 hours to about 28 days after the first oral dosage form is administered.

~~29. The oral dosage form of any of claims 15-28, wherein the zoledronic acid in the oral dosage form has a 24 hour sustained plasma level factor of about 1 or higher.~~

~~30. The oral dosage form of any of claims 15-28, wherein the zoledronic acid in the oral dosage form has a 24 hour sustained plasma level factor that is higher than that of intravenously administered zoledronic acid.~~

CLAIMS

1. A method of preparing an oral dosage form having enhanced oral bioavailability of zoledronic acid comprising: mixing a disodium salt form of zoledronic acid with an excipient; wherein the method results in a disodium salt form of zoledronic acid in the dosage form that has an enhanced oral bioavailability in a mammal as compared to a diacid form of zoledronic acid.

2. The method of claim 1, wherein the dosage form has an oral bioavailability that results in an area under the plasma concentration curve of zoledronic acid of about 4 ng·h/mL to about 2000 ng·h/mL if the dosage form is administered to the mammal.

3. The method of claim 2, wherein the dosage form has an oral bioavailability that results in an area under the plasma concentration curve of zoledronic acid of about 100 ng·h/mL to about 2000 ng·h/mL if the dosage form is administered to the mammal.

4. The method of claim 2, wherein the dosage form has an oral bioavailability that results in an area under the plasma concentration curve of zoledronic acid of about 20 ng·h/mL to about 700 ng·h/mL if the dosage form is administered to the mammal.

5. The method of claim 2, wherein the dosage form is produced as a solid comprising at least about 50% (w/w) of zoledronic acid.

6. The method of claim 2, wherein the dosage form is suitable for administration at an interval of about 3 to about 4 weeks.

7. The method of claim 1, wherein the dosage form is prepared in a form that is suitable to be administered weekly, or 3 to 5 times in a month, wherein the dosage form has an oral bioavailability that results in an area under the plasma concentration curve of zoledronic acid of about 20 ng·h/mL to about 700 ng·h/mL if the dosage form is administered to the mammal.

8. The method of claim 1, wherein the dosage form is prepared in a form that is suitable to be administered daily, wherein the dosage form has an oral bioavailability that results in an area under the plasma concentration curve of zoledronic acid of about 4 ng·h/mL to about 100 ng·h/mL if the dosage form is administered to the mammal.

9. The method of claim 1, wherein the dosage form is a solid.

10. The method of claim 1, wherein the oral bioavailability of dosage form in the mammal is improved by at least about 20% as compared to administration of zoledronic acid in the diacid form.

11. The method of claim 1, wherein the dosage form comprises, on a molar basis, less of the zoledronic acid in the disodium salt form than would be present of zoledronic acid in the diacid form in order to achieve the same plasma levels of zoledronic acid.

12. The method of claim 1, wherein the dosage form comprises at least about 10 mole % less of the disodium salt form as compared to the amount of zoledronic acid in the diacid form that would be administered in order to achieve the same plasma levels of zoledronic acid in the mammal.

13. The method of claim 1, wherein the dosage form comprises the disodium salt form in an amount, on a molar basis, that has a value of about $0.8n_d$ to about $1.2n_d$, wherein:

$$n_d=(b_a/b_d)(n_a)$$

wherein b_a is the oral bioavailability of the diacid form, b_d is the oral bioavailability of the disodium salt form, and n_a is the number of moles of zoledronic acid in the diacid form that would be administered in order to achieve the same plasma levels of zoledronic acid in the mammal.