CLAIMS

1. A dendrimer comprising:

i) a core unit (C); and

ii) building units (BU), each building unit being a lysine residue or an analogue thereof;

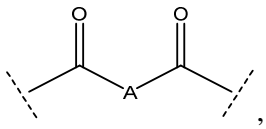
wherein the core unit is covalently attached to two building units *via* amide linkages, each amide linkage being formed between a nitrogen atom present in the core unit and the carbon atom of an acyl group present in a building unit;

the dendrimer being a five generation building unit dendrimer;

wherein building units of different generations are covalently attached to one another *via* amide linkages formed between a nitrogen atom present in one building unit and the carbon atom of an acyl group present in another building unit;

the dendrimer further comprising:

iii) a plurality of first terminal groups (T1) each comprising a residue of a nucleoside analogue, which nucleoside analogue has a hydroxyl group, covalently attached to a diacyl linker group of formula:



, wherein A is a C_2-C_{10} alkylene group which is interrupted by at least one O, S, NH, or N(Me), or in which A is a heterocycle selected from the group consisting of tetrahydrofuran, tetrahydrothiophene, pyrrolidine, and N-methylpyrrolidine; and

iv) a plurality of second terminal groups (T2) each comprising a hydrophilic polymeric group;

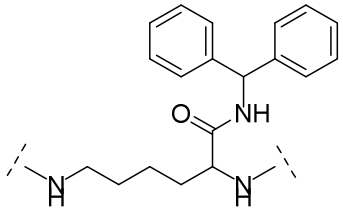
or a pharmaceutically acceptable salt thereof.

2. A dendrimer as claimed in claim 1, wherein the nucleoside analogue is selected from the group consisting of gemcitabine, cytarabine, and azacitadine.

3. A dendrimer as claimed in claim 2, wherein the nucleoside analogue is gemcitabine.

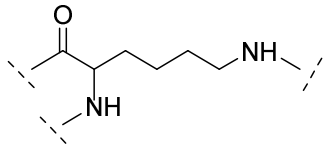
4. A dendrimer as claimed in any one of claims 1 to 3, wherein the core unit is formed from a core unit precursor comprising two amino groups.

5. A dendrimer as claimed in any one of claims 1 to 4, wherein the core unit is:



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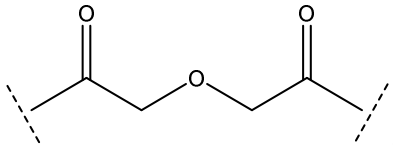
6. A dendrimer as claimed in any one of claims 1 to 5, wherein the building units are each:



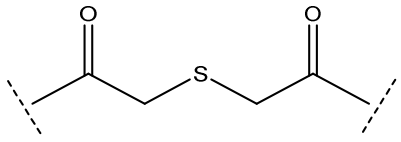
;

wherein the acyl group of each building unit provides a covalent attachment point for attachment to the core or to a previous generation building unit; and wherein each nitrogen atom provides a covalent attachment point for covalent attachment to a subsequent generation building unit, a first terminal group or a second terminal group.

7. A dendrimer as claimed in any one of claims 1 to 6, wherein the diacyl linker is selected from the group consisting of:

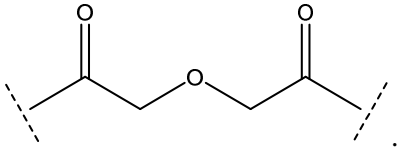


and



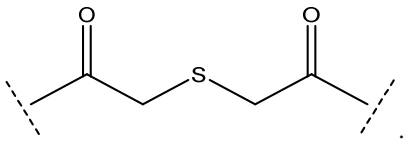
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8. A dendrimer as claimed in any one of claims 1 to 7, wherein the diacyl linker is



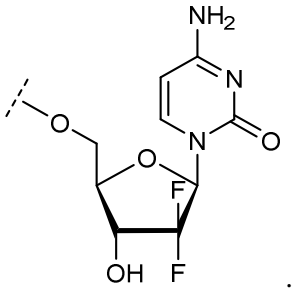
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9. A dendrimer as claimed in any one of claims 1 to 7, wherein the diacyl linker is



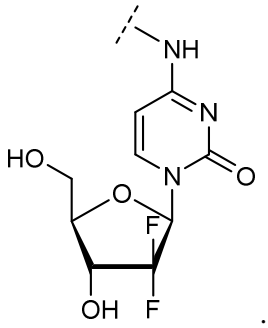
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10. A dendrimer as claimed in any one of claims 1 to 9, wherein the nucleoside analogue is gemcitabine and is covalently attached to the diacyl linker group as shown below:



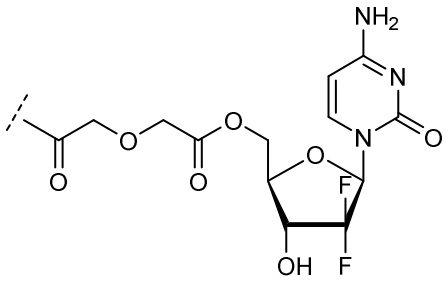
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11. A dendrimer as claimed in any one of claims 1 to 9, wherein the nucleoside analogue is gemcitabine and is covalently attached to the diacyl linker group as shown below:



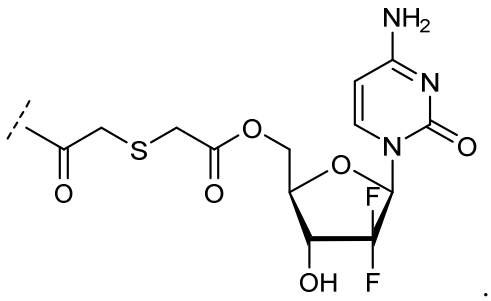
.

12. A dendrimer as claimed in claim 10, wherein the first terminal group is:



.

13. A dendrimer as claimed in claim 10, wherein the first terminal group is:



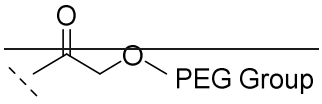
.

14. A dendrimer as claimed in any one of claims 1 to 13, wherein the hydrophilic polymeric group is selected from the group consisting of polyethylene glycol (PEG), polyethyloxazoline (PEOX), and polysarcosine.

15. A dendrimer as claimed in any one of claims 1 to 14, wherein the second terminal groups comprise PEG groups having a mean molecular weight of at least 500 Daltons.

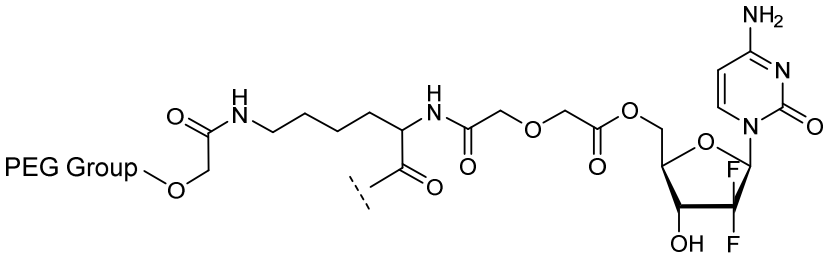
~~16. A dendrimer as claimed in any of claims 1 to 15, wherein the second terminal groups each comprise a PEG group covalently attached to a PEG linking group (L1) *via* an ether linkage formed between a carbon atom present in the PEG group and an oxygen atom present in the PEG linking group, and each second terminal group is covalently attached to a building unit *via* an amide linkage formed between a nitrogen atom present in a building unit and the carbon atom of an acyl group present in the PEG linking group.~~

~~17. A dendrimer as claimed in claim 16, wherein the second terminal groups are each~~

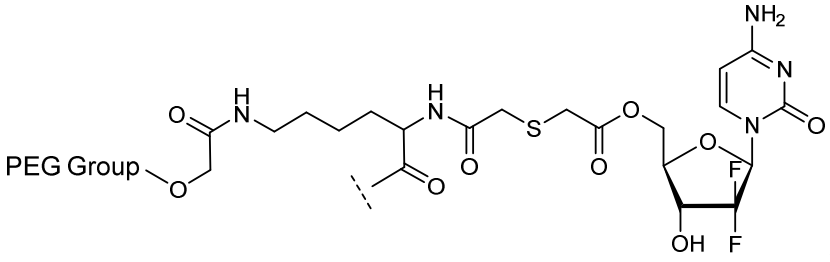


~~and wherein the PEG group is a methoxy-terminated PEG having an average molecular weight in the range of from 500 to 2500 Daltons.~~

~~18~~16. A dendrimer as claimed in ~~claim 17~~any one of claims 1 to 15, wherein the dendrimer comprises surface units comprising an outer building unit attached to a first terminal group and a second terminal group, the surface units having the structure:



or



,

and wherein the PEG group is a methoxy-terminated PEG having an average molecular weight in the range of from 500 to 2500 Daltons.

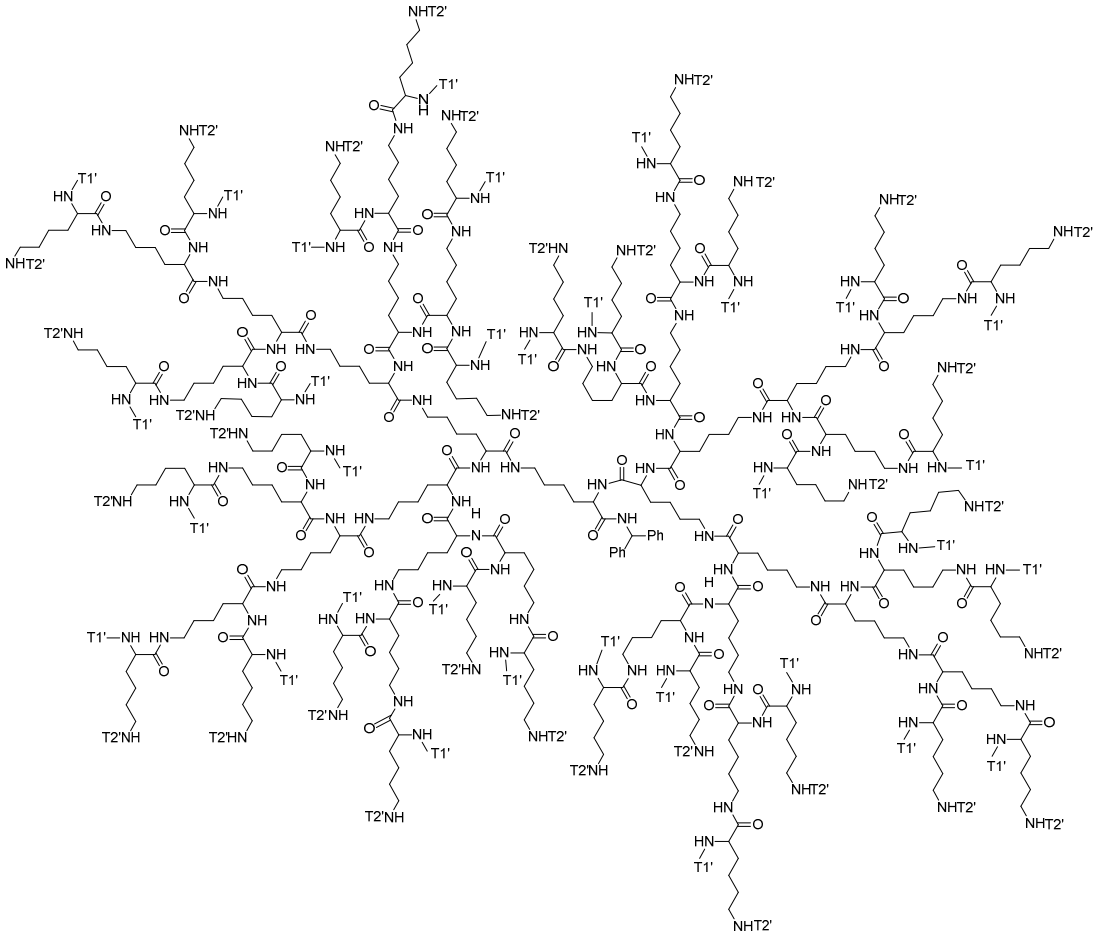
~~19. A dendrimer as claimed in claim 18, wherein the dendrimer has from 28 to 32 surface units.~~

~~20. A dendrimer as claimed in any of claims 1 to 19, wherein at least 40% of the nitrogen atoms present in the outer building units are each covalently attached to a first terminal group; and at least 40% of the nitrogen atoms present in the outer building units are each covalently attached to a second terminal group.~~

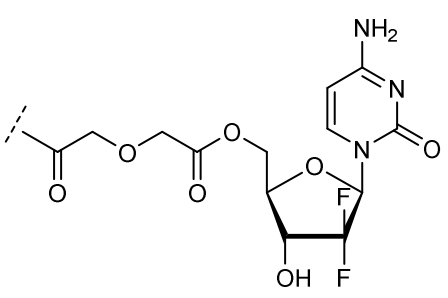
~~21. A dendrimer as claimed in any of claims 1 to 18 or 20, wherein the five generations of building units are complete generations, and wherein the outer generation of building units provides 64 nitrogen atoms for covalent attachment to a first terminal group or a second terminal group, wherein from 24 to 32 first terminal groups are covalently attached to one of said nitrogen atoms, and wherein from 24 to 32 second terminal groups are each covalently attached to one of said nitrogen atoms.~~

~~22. A dendrimer as claimed in any of claims 1 to 21, wherein when the dendrimer is exposed to PBS at pH 7.4 and 37 °C, between about 20% and about 90% of the residue of the nucleoside analogue is released from the dendrimer after 24 hours.~~

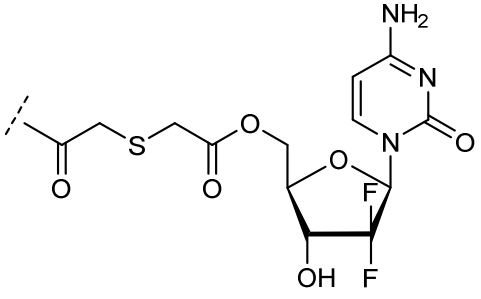
~~23~~17. A dendrimer as claimed in any one of claims 1 to ~~22~~16, wherein the dendrimer is:



in which T1′ represents a first terminal group which is

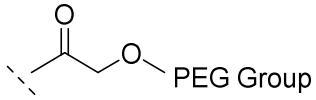


or



; and

T2′ represents a second terminal group which is



wherein the PEG group is a methoxy-terminated PEG having an average molecular weight in the range of from 500 to 2500 Daltons, or T2′ represents H, and wherein less than 5 of T2′ are H.

24. A dendrimer as claimed in any of claims 1 to 23, wherein the second terminal groups comprise PEG groups having an average molecular weight in the range of from 1900 to 2300 Daltons.

2518. A pharmaceutical composition comprising:
i) a dendrimer as claimed in any one of claims 1 to 2417, or a pharmaceutically acceptable salt thereof; and ii) a pharmaceutically acceptable excipient.

26. A dendrimer as claimed in any of claims 1 to 24, or a pharmaceutical composition as claimed in claim 25, for use in the treatment of cancer.

27. A method of treating cancer comprising administering to a subject in need thereof a therapeutically effective amount of a dendrimer according to any of claims 1 to 24 or a pharmaceutical composition according to claim 25 or claim 26.

2819. Use of a dendrimer as claimed in any one of claims 1 to 2417, or of a pharmaceutical composition as claimed in any of claims 1825 to 27, in the manufacture of a medicament for the treatment of cancer.

2920. A method,The use, or dendrimer or composition for use, as claimed in any of claims 26 to 28claim 19, wherein the cancer is selected from the group consisting of breast cancer, ovarian cancer, non-small cell lung cancer, an upper gastrointestinal cancer (e.g. pancreatic cancer), and bladder cancer.

3021. A method,The use, or dendrimer or composition for use as claimed in any of claims 26 19 or 20to 29, wherein the amount of dendrimer administered is sufficient to deliver an amount of active agent in the range of from 5 mg to 200 mg of nucleoside analogue/m^2.

~~31~~22. ~~A method,~~The use~~, or dendrimer or composition for use~~ as claimed in any one of claims ~~26~~ 19 to ~~30~~21, wherein the dendrimer is to be administered in combination with a further anticancer agent.

~~32~~23. ~~A method,~~The use~~, or dendrimer or composition for use~~ as claimed in claim ~~31~~22, wherein the further anticancer agent is selected from the group consisting of platinum-containing pharmaceutical agents, taxanes, immunooncology agents, PARP inhibitors, topoisomerase I inhibitors, antibodies, antifolates, tyrosine kinase inhibitors, anthracyclines, and vinca alkaloids.

~~33~~24. ~~A method,~~The use~~, or dendrimer or composition for use~~ as claimed in claim ~~32~~23, wherein the dendrimer is to be administered in combination with a further anticancer agent selected from the group consisting of capecitabine, Nab-paclitaxel (e.g. Abraxane®), docetaxel, cabazitaxel, doxorubicin, vindesine, irinotecan, folinic acid, 5-fluorouracil, methotrexate, pemetrexed, lapatinib, nintedanib, sunitinib, olaparib, niraparib, carboplatin, paclitaxel, SN38, cisplatin, oxaliplatin, paclitaxel, erlotinib, and irinotecan.

~~34. A method, use, or dendrimer or composition for use as claimed in claim 30, wherein the dendrimer is administered in combination with a second dendrimer, and wherein the second dendrimer comprises:~~

~~i) a core unit (C); and~~

~~ii) building units (BU), each building unit being a lysine residue or an analogue thereof;~~

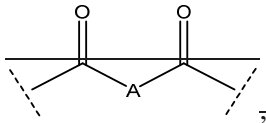
~~wherein the core unit is covalently attached to two building units *via* amide linkages, each amide linkage being formed between a nitrogen atom present in the core unit and the carbon atom of an acyl group present in a building unit;~~

~~the dendrimer being a five generation building unit dendrimer;~~

~~wherein building units of different generations are covalently attached to one another *via* amide linkages formed between a nitrogen atom present in one building unit and the carbon atom of an acyl group present in another building unit;~~

~~the dendrimer further comprising:~~

iii) a plurality of first terminal groups (T1) each comprising a residue of n oncology agent, which oncology agent has a hydroxyl group, covalently attached to a diacyl linker group of formula:



, wherein A is a C_2-C_{10} alkylene group which is interrupted by at least one O, S, NH, or N(Me), or in which A is a heterocycle selected from the group consisting of tetrahydrofuran, tetrahydrothiophene, pyrrolidine, and N-methylpyrrolidine; and

iv) a plurality of second terminal groups (T2) each comprising a hydrophilic polymeric group;

or a pharmaceutically acceptable salt thereof.

35. A method, use, or dendrimer or composition for use as claimed in claim 34, wherein the oncology agent is a taxane.

36. A method, use, or dendrimer or composition for use as claimed in claim 35, wherein the taxane is selected from the group consisting of docetaxel, paclitaxel and cabazitaxel.

37. A method, use, or dendrimer or composition for use as claimed in any of claims 34 to 36, wherein the taxane is docetaxel.

38. A method, use, or dendrimer or composition for use as claimed in claim 34, wherein the oncology agent is a topoisomerase I inhibitor.

39. A method, use, or dendrimer or composition for use as claimed in claim 38, wherein the topoisomerase I inhibitor is SN-38.

40. A method, use, or dendrimer or composition for use as claimed in any of claims 34 to 39, wherein the dendrimer is administered in combination with a further anticancer agent.

41. A method, use, or dendrimer or composition for use as claimed in claim 40, wherein the further anticancer agent is selected from the group consisting of platinum containing

pharmaceutical agents, taxanes, immunooncology agents, PARP inhibitors, topoisomerase I inhibitors, antibodies, antifolates, tyrosine kinase inhibitors, anthracyclines, and vinca alkaloids.

42. A method, use, or dendrimer or composition for use as claimed in claim 41, wherein the further anticancer agent is selected from the group consisting of capecitabine, Nab paclitaxel (e.g. Abraxane®), docetaxel, cabazitaxel, doxorubicin, vindesine, irinotecan, folinic acid, 5-fluorouracil, methotrexate, pemetrexed, lapatinib, nintedanib, sunitinib, olaparib, niraparib, carboplatin, paclitaxel, SN38, cisplatin, oxaliplatin, paclitaxel, erlotinib, and irinotecan.

43. A method, use, or dendrimer or composition for use as claimed in any of claims 34 to 42, wherein administration of the dendrimer provides enhanced clinical efficacy in comparison to administration of an equivalent dose of free nucleoside analogue.

44. A method, use, or dendrimer or composition for use as claimed in any of claims 34 to 43, wherein administration of the dendrimer provides reduced side effects and/or toxicity in comparison to administration of an equivalent dose of free nucleoside analogue.

45. A method, use, or dendrimer or composition for use as claimed in any of claims 34 to 44, wherein administration of the dendrimer provides therapeutically effective plasma concentration levels of gemcitabine for an extended period of time following administration, in comparison to administration of an equivalent dose of free nucleoside analogue.