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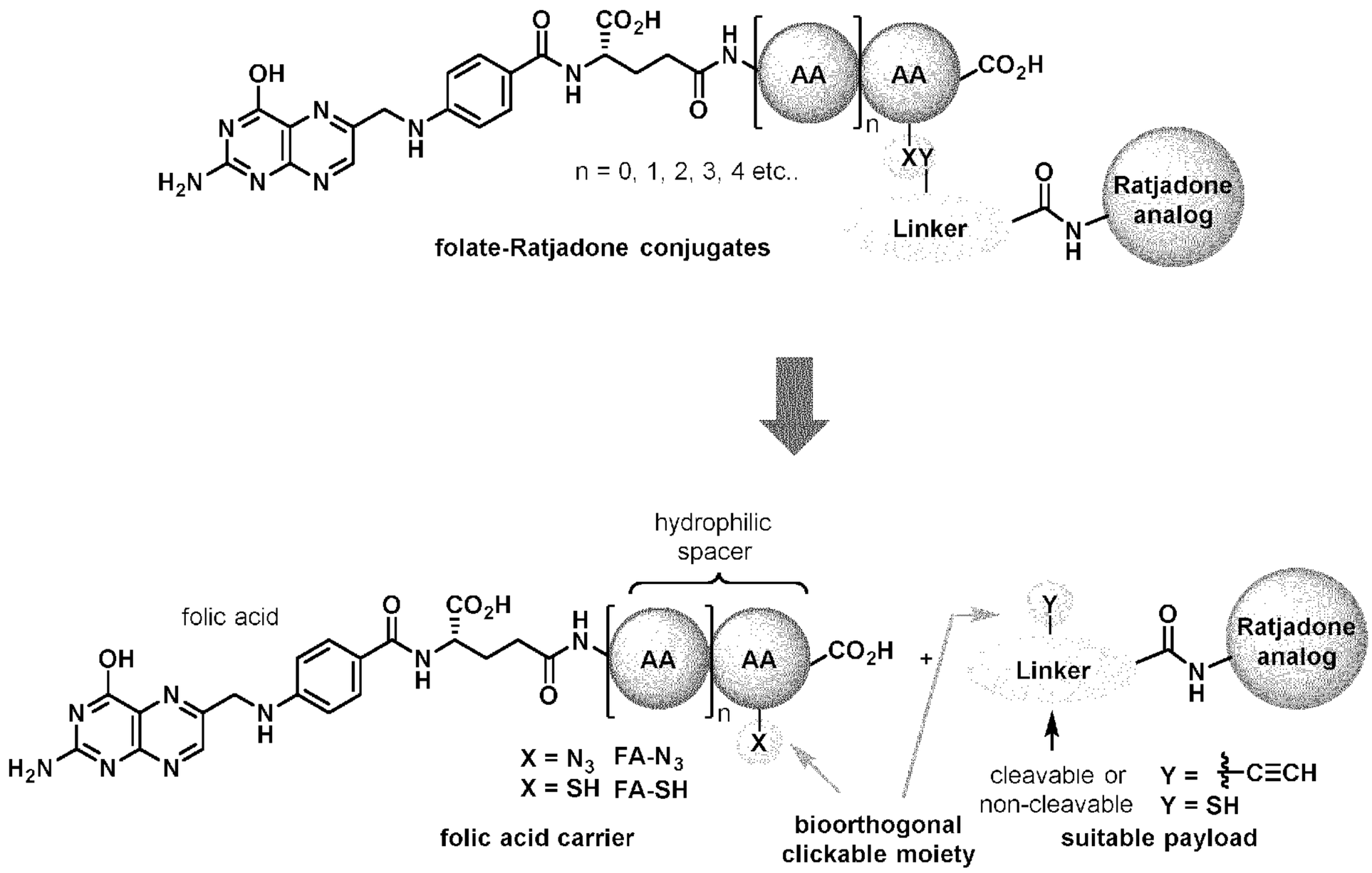
(54) Titre : NOUVEAUX DERIVES DE RATJADONE CYTOTOXIQUES CIBLES ET LEURS CONJUGUES
(54) Title: NEW TARGETED CYTOTOXIC RATJADONE DERIVATIVES AND CONJUGATES THEREOF

**FIGURE 2:**




(57) Abrégé/Abstract:
The present invention is directed to novel natural product-derived ratjadone-based compounds useful as payloads (or toxins) in drug-conjugates constructs with cell target binding moieties (CTBM) and payload-linker compounds useful in connection with drug conjugates. The present invention further relates to new ratjadone compositions including the aforementioned payloads, payload-linkers and drug conjugates, and methods for using these payloads, payload-linkers and drug conjugates, to treat pathological conditions including cancer, inflammatory and infectious diseases.

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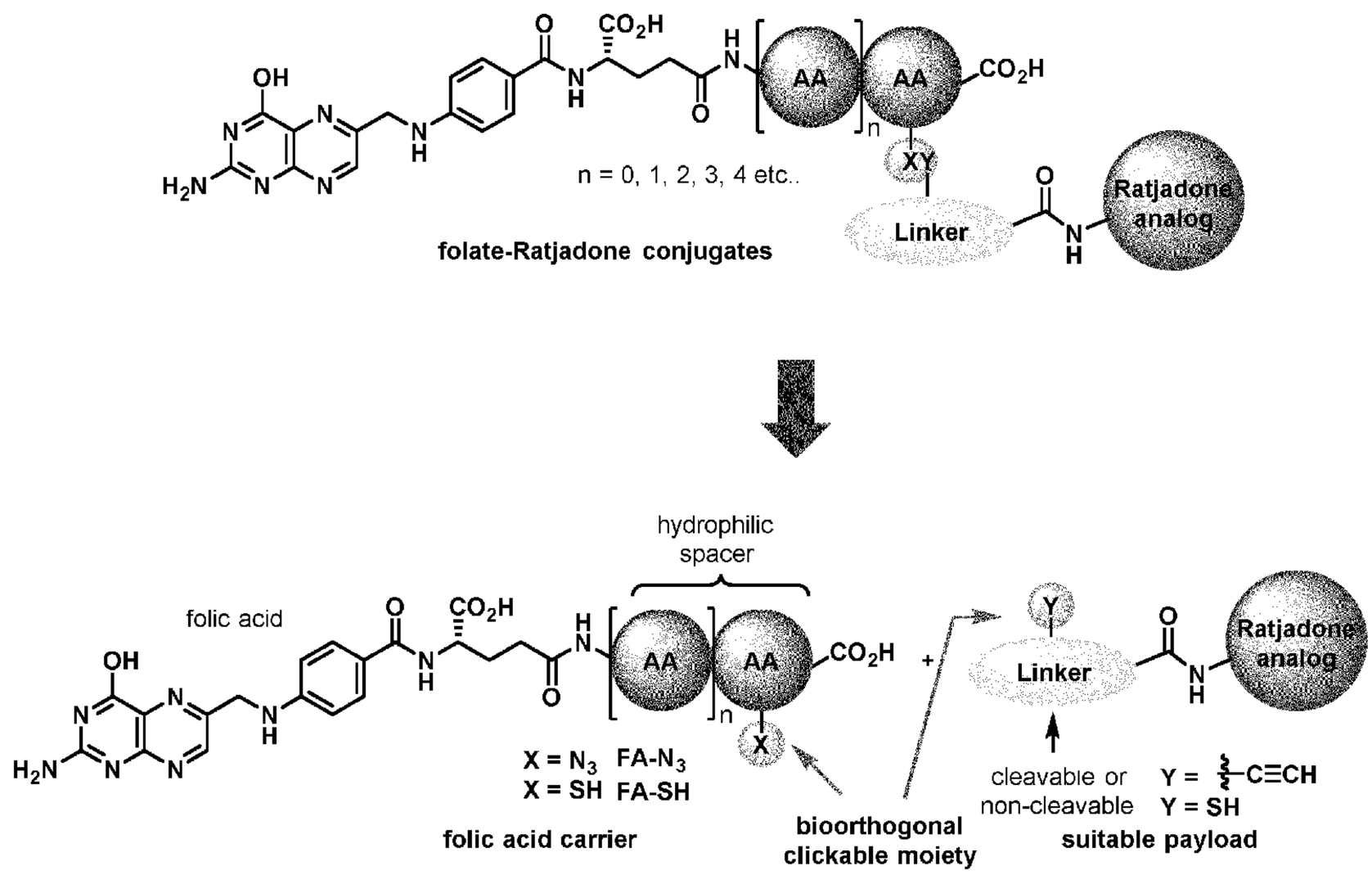
(54) Title: NEW TARGETED CYTOTOXIC RATJADONE DERIVATIVES AND CONJUGATES THEREOF

**FIGURE 2:**




(57) Abstract: The present invention is directed to novel natural product-derived ratjadone-based compounds useful as payloads (or toxins) in drug-conjugates constructs with cell target binding moieties (CTBM) and payload-linker compounds useful in connection with drug conjugates. The present invention further relates to new ratjadone compositions including the aforementioned payloads, payload-linkers and drug conjugates, and methods for using these payloads, payload-linkers and drug conjugates, to treat pathological conditions including cancer, inflammatory and infectious diseases.

*[Continued on next page]*

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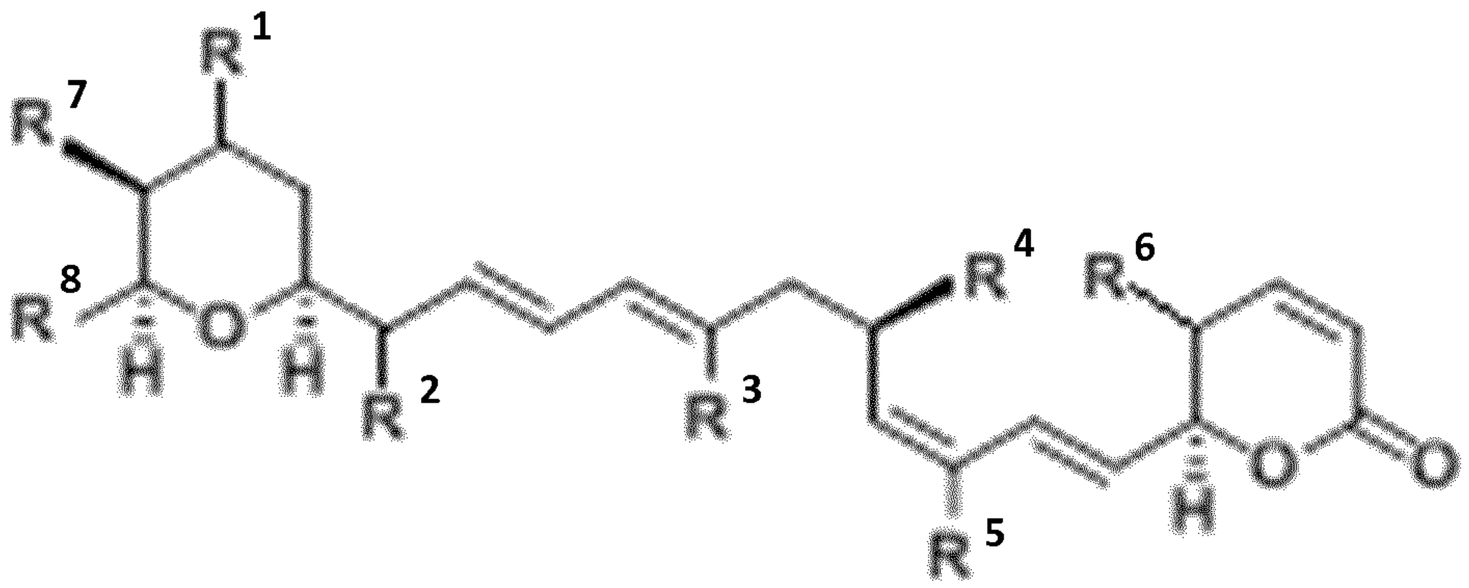
# CLAIMS

1. A compound according to Formula I



I

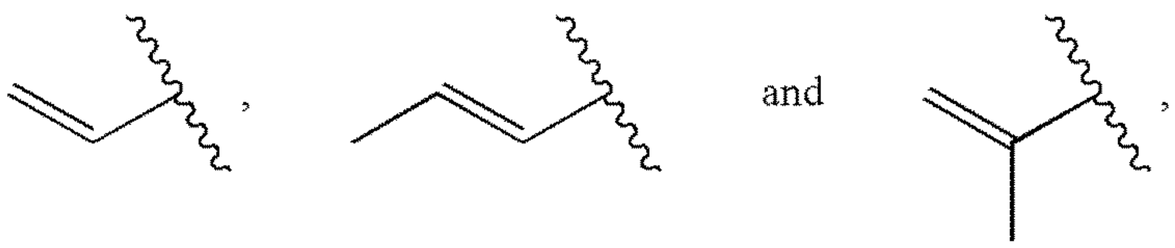
wherein:

one of $R^1$ and $R^2$ is $NHR^9$ and one is selected from H and OH;

$R^3$, $R^4$ and $R^5$ are independently of one another selected from the group that consists of H, $CH_3$ and $C_2H_5$;

$R^6$ is $CH_3$ or $C_2H_5$;

$R^7$ and $R^8$ are independently of one another selected from the group that consists of H, $CH_3$, $C_2H_5$, n-$C_3H_7$,



; and

$R^9$ is H.

2. A compound according to Formula I, wherein:

$R^1$ to $R^8$ are as defined in claim 1; and

$R^9$ is L-RM*, wherein L is a linker, particularly a self-immolative linker, RM* is selected from RM and RM', wherein RM is a reactive moiety being able to form a covalent bond with a targeting moiety, particularly a target-binding antibody or functional fragment thereof, and wherein RM' is a moiety RM carrying a protecting group.

3. A compound according to Formula I, wherein:

$R^1$ to $R^8$ are as defined in claim 1; and
$R^9$ is L-TM, wherein L is a linker, particularly a self-immolative linker, and TM is a targeting moiety.

4. The compound of any one of claims 1 to 3, wherein $R^1$ is OH and $R^2$ is $NHR^9$.

5. The compound of claim 4, wherein $R^2$ is 16*R*-$NHR^9$.

6. The compound of claim 4, wherein $R^2$ is 16*S*-$NHR^9$.

7. The compound of any one of claims 1 to 3, wherein $R^1$ is $NHR^9$ and $R^2$ is OH.

8. A method of synthesizing a compound according to claim 2, comprising the step of reacting a compound according to claim 1 via the amino group $R^1$ or $R^2$ with a compound X-L'-RM*, wherein

X is a group that is (i) able to react with an amine, or (ii) can be replaced by an amine; and
L' is a linker;
wherein the reaction of said amino group with the moiety X-L' results in the formation of the moiety –NH-L-RM*.

9. The method according to claim 8, wherein RM* is RM', further comprising the deprotection of the moiety RM' to result in RM.

10. A method of synthesizing a compound according to claim 3, comprising the step of reacting a compound according to claim 2 with a targeting moiety.

11. A pharmaceutical composition comprising the compound according to claim 3 or a compound synthesized according to the method according to claim 10.

12. The pharmaceutical composition according to claim 11 for use in the treatment of cancer.

13. A method for the treatment of cancer comprising the step of administering the compound according to claim 3, or the pharmaceutical composition according to claim 11 or 12, to a patient in need of such treatment.