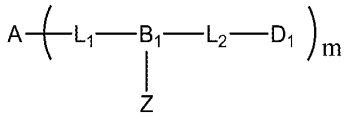
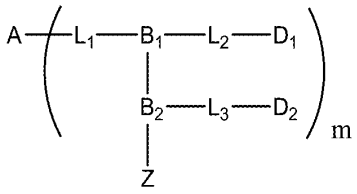
权 利 要 求 书

1. 一种如式（Ⅰ）—（Ⅳ）所示的抗体药物偶联物：



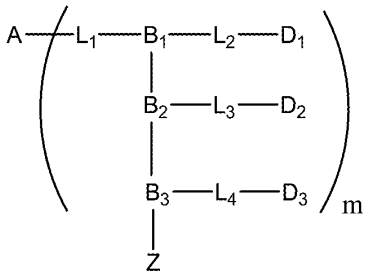
（Ⅰ）

或



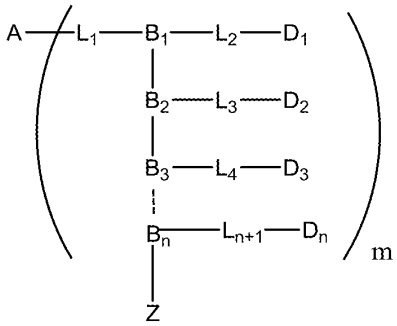
（Ⅱ）

或



（Ⅲ）

或



（Ⅳ）

其中：

A 为任一抗体或其功能性结合片段；

B_1、B_2、B_3、……、B_n 为半胱氨酸残基或半胱氨酸衍生物残基，可相同也可以不同，B_1 与 B_2、B_2 与 B_3、……、B_{n-1} 与 B_n 通过脱水缩合形成的肽键连接；

L_1、L_2、L_3、L_4、……、L_{n+1} 为任一连接单元且相互独立，可相同也

可以不同，所述 L_1 与 B_1 中氨基端共价相连，所述 L_2 与 B_1、L_3 与 B_2、L_4 与 B_3、……、L_{n+1} 与 B_n 是通过巯基共价连接，所述 L_2 与 D_1、L_3 与 D_2、L_4 与 D_3、……、L_{n+1} 与 D_n 共价相连；

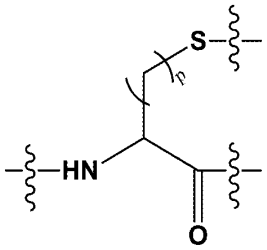
D_1、D_2、D_3、……、D_n 是任一活性药物单元且相互独立，可相同也可以不同；

Z 为任一基团，共价连接于式（Ⅰ）中 B_1 的羰基上或式（Ⅱ）中 B_2 的羰基上或式（Ⅲ）中 B_3 的羰基上或式（Ⅳ）中 B_n 的羰基上；

n 为大于或等于 4 的整数，代表连接活性药物单元支链的数量；

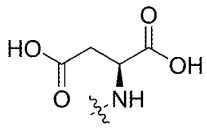
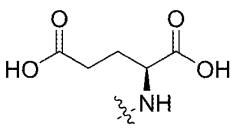
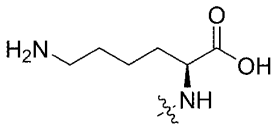
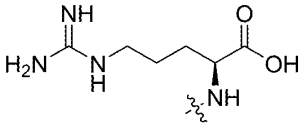
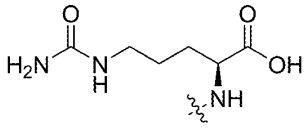
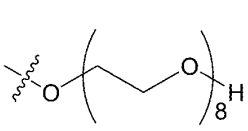
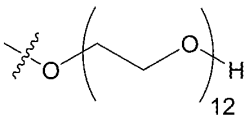
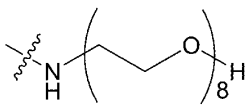
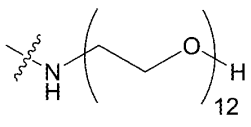
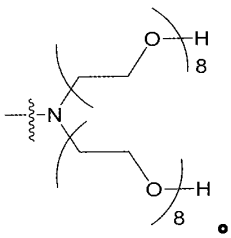
m 选自 1、2、3、4、5、6、7、8。

2. 根据权利要求 1 所述的抗体药物偶联物，其特征在于，所述的 B_1、B_2、B_3、.....、B_n 的结构分别如式（V）所示：

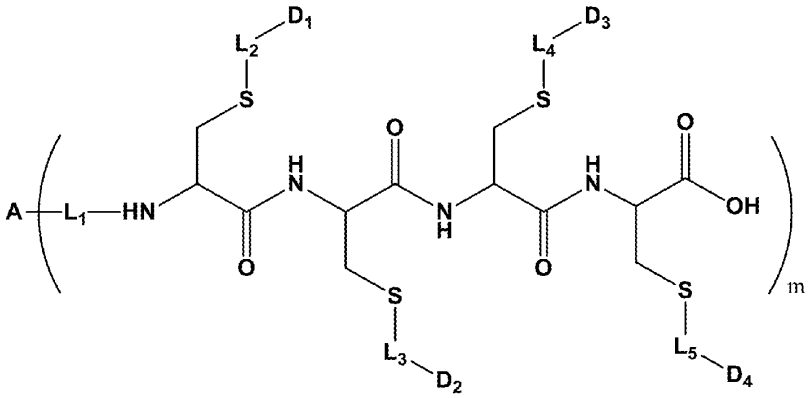

(V)

其中，p 选自 1、2、3、4、5、6、7、8。

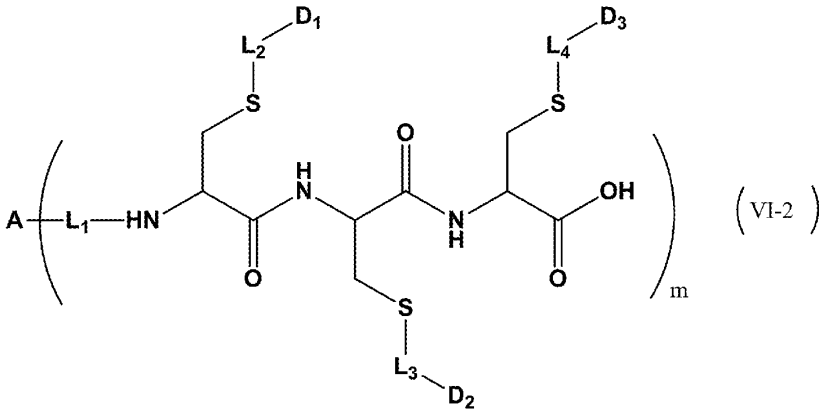
3. 根据权利要求 1 所述的抗体药物偶联物，其特征在于，所述的 Z 选自：

OH、SH、NH_2、  、  、  、  、  、  、  、  、  、  。

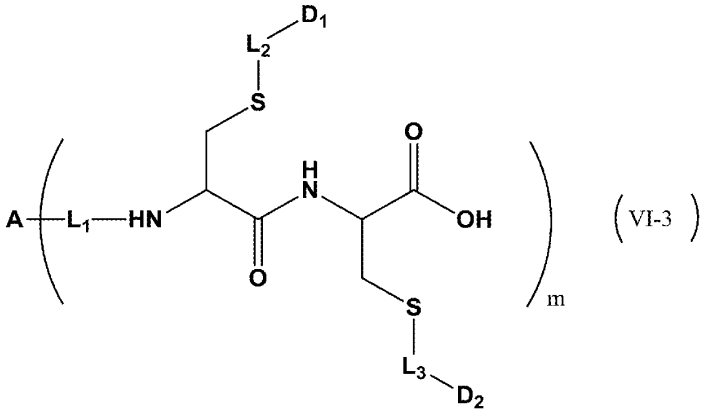
4. 根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于，所述的抗体药物偶联物具有式（VI-1）-（VI-5）所示的结构：



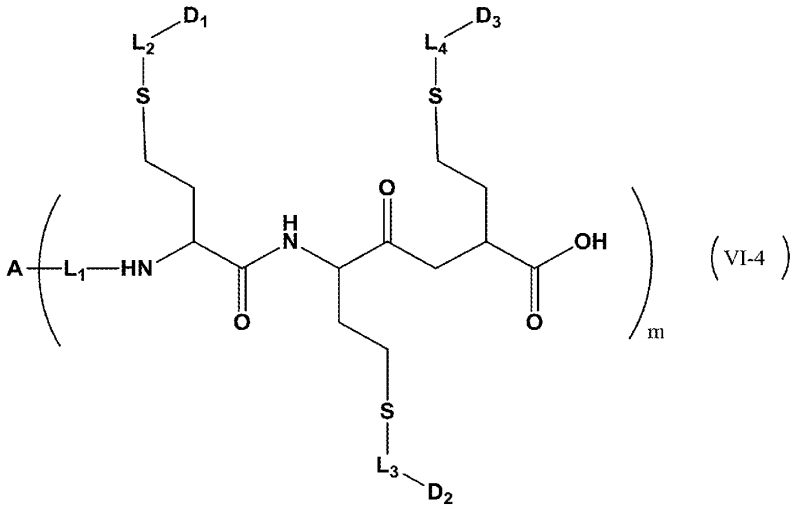
(VI-1)



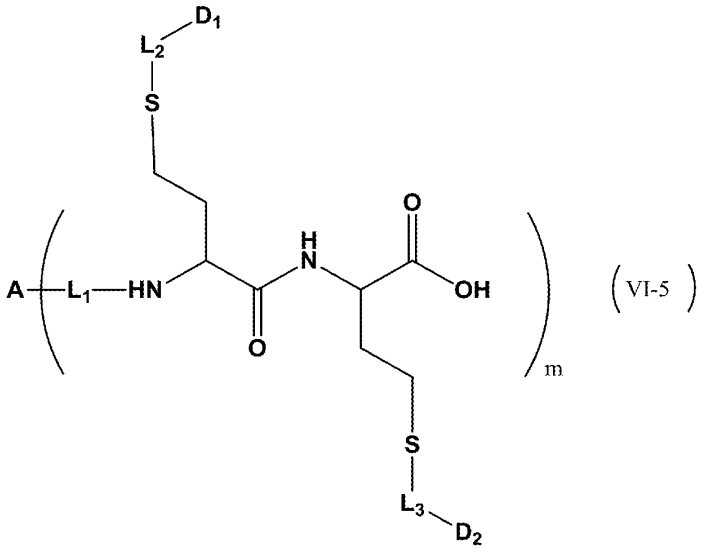
(VI-2)



(VI-3)



(VI-4)



(VI-5)

其中：

A 为任一抗体或其功能性结合片段；

L_1、L_2、L_3、L_4、L_5 为任一连接单元且相互独立，可相同也可以不同；

D_1、D_2、D_3、D_4 是任一活性药物单元且相互独立，可相同也可以不同；

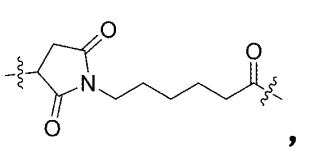
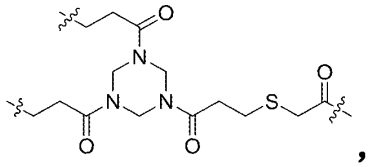
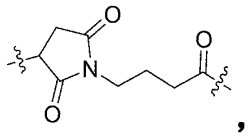
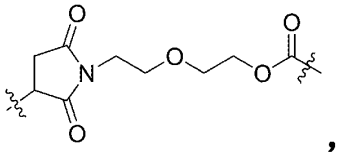
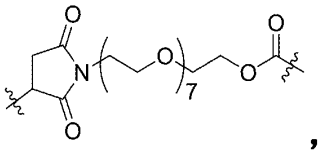
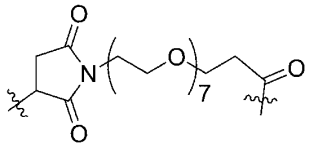
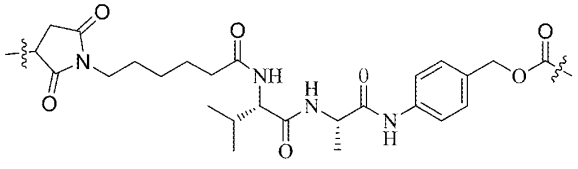
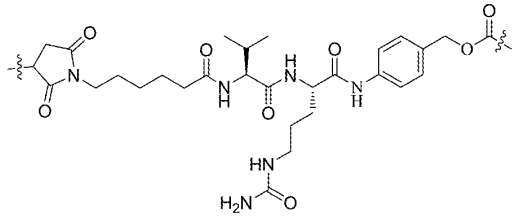
m 选自 1、2、3、4、5、6、7、8。

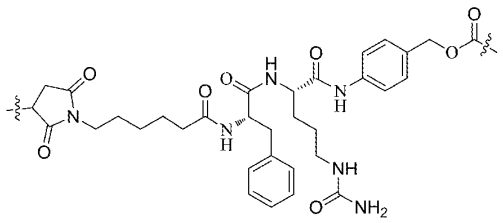
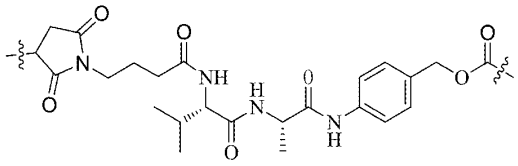
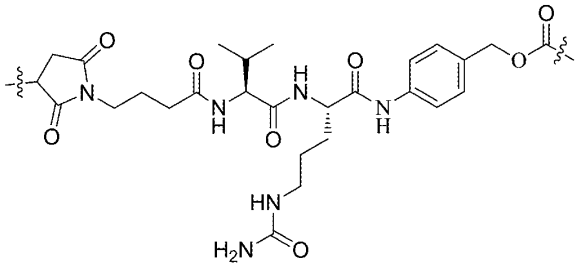
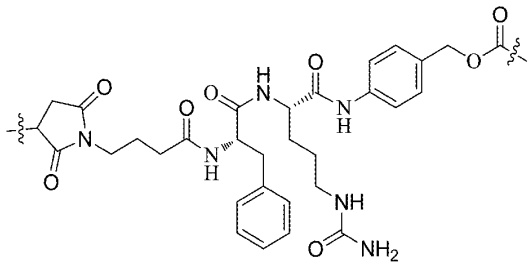
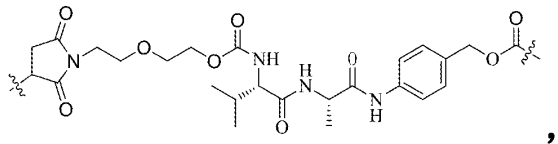
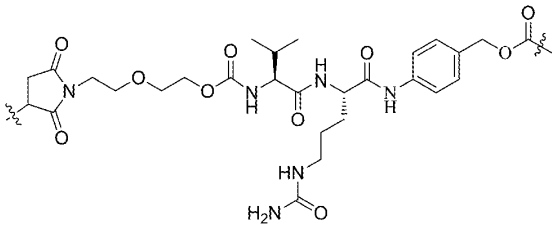
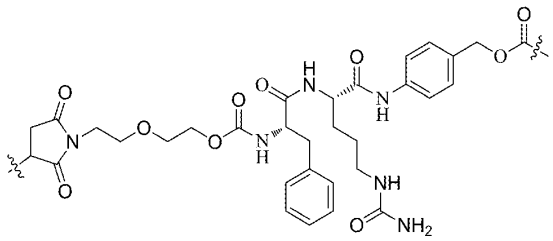
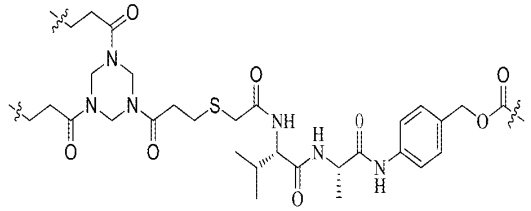
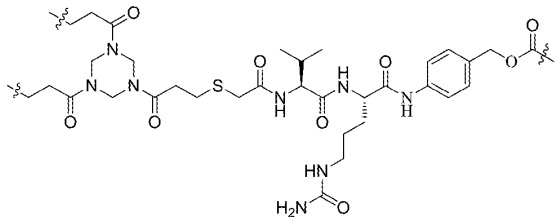
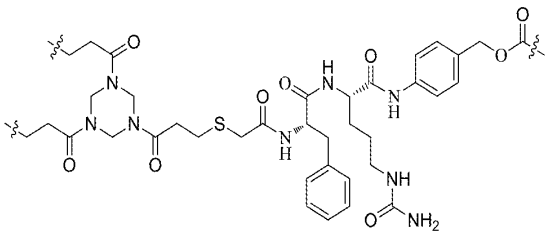
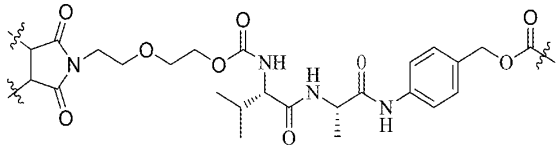
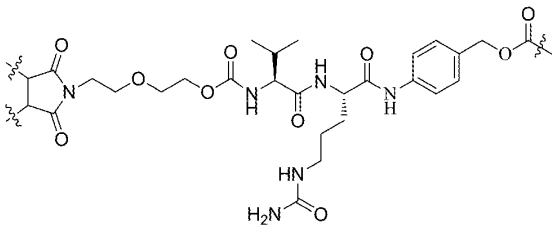
5. 根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于：所述 L_1 与抗体上氨基残基或巯基残基共价连接；优选的，所述 L_1 与抗体上的巯基残基共价连接；更优选的，所述 L_1 与抗体上的链间二硫键打开后形成的巯基残基共价连接。

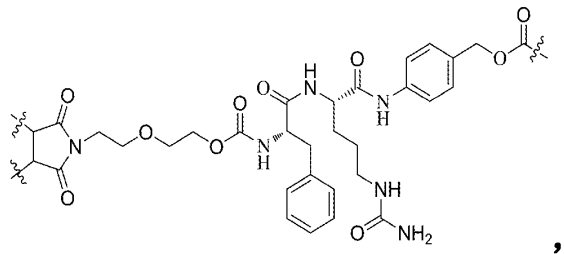
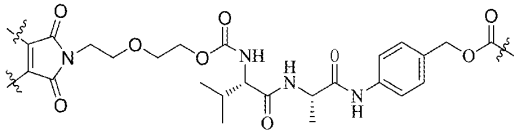
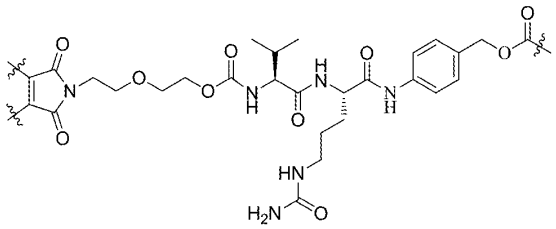
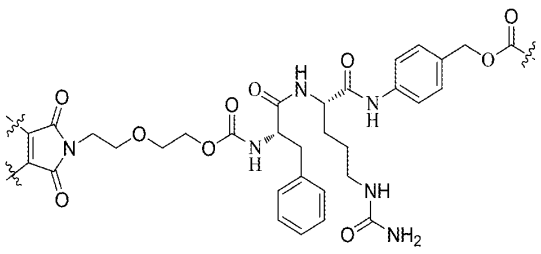
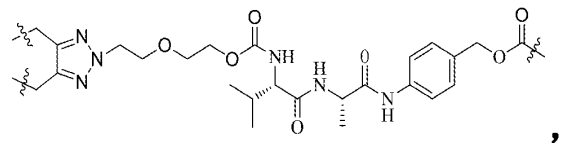
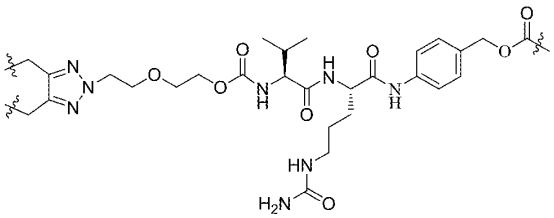
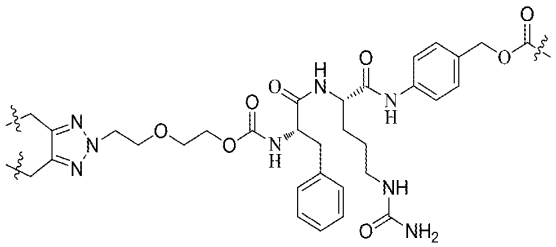
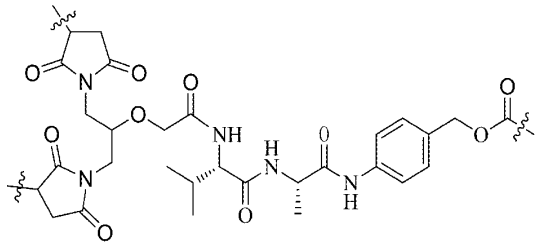
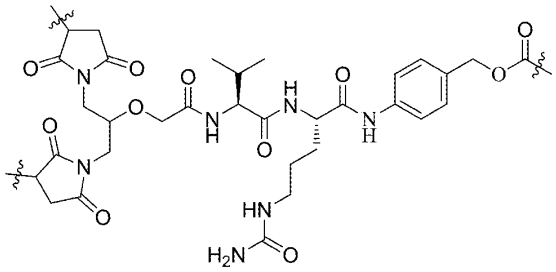
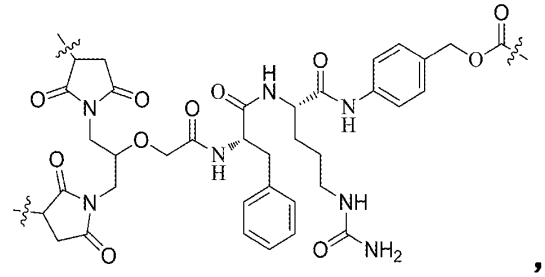
6. 根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于：所述 L_1、L_2，L_3，L_4、……、L_{n+1} 为可裂解连接子、可裂解连接子组合或不可裂解连接子。

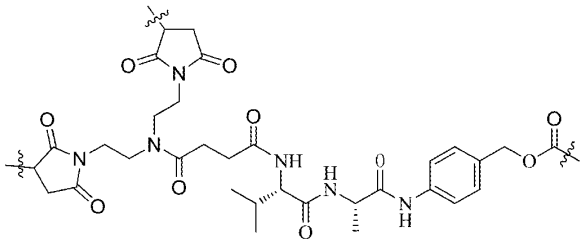
7. 根据权利要求 6 所述的抗体药物偶联物，其特征在于：所述的可裂解的连接子包括肽单元和多硫键，所述的肽单元包含 2-20 个氨基酸，优选的所述的肽单元选自由-缬氨酸-瓜氨酸-（-Val-Cit-）、-甘氨酸-甘氨酸-苯丙氨酸-甘氨酸-（-Gly-Gly-Phe-Gly-）、-缬氨酸-丙氨酸-（-Val-Ala-）、-缬氨酸-赖氨酸-（-Val-Lys-）、-缬氨酸-精氨酸-（-Val-Arg-）、-苯丙氨酸-瓜氨酸-（-Phe-Cit-）、-苯丙氨酸-赖氨酸-（-Phe-Lys-）、-苯丙氨酸-精氨酸-（-Phe-Arg-）及它们的组合；所述的多硫键包含 2-8 个硫原子，优选的所述的多硫键选自于二硫键（-S-S-）、三硫键（-S-S-S-）、四硫键（-S-S-S-S-）。

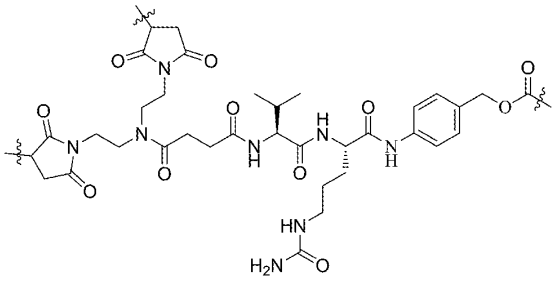
8. 根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于，所述的 L_1 包括以下结构：

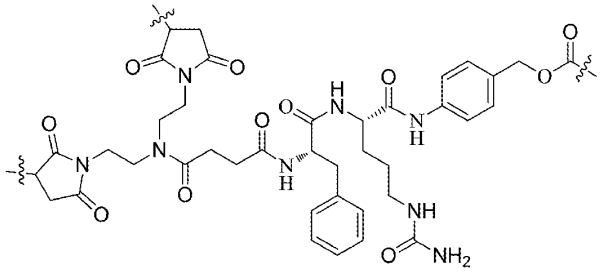

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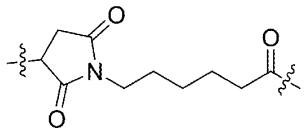

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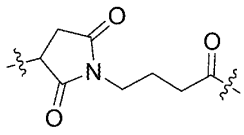

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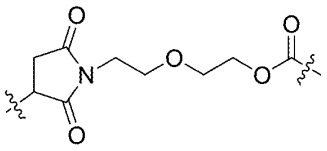

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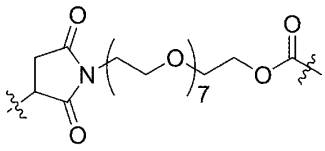

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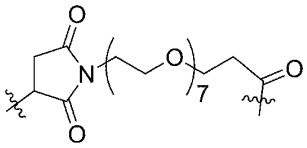
9. 根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于，所述的 L_2，L_3，L_4、……、L_{n+1} 包括以下结构：

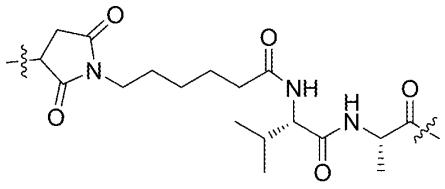

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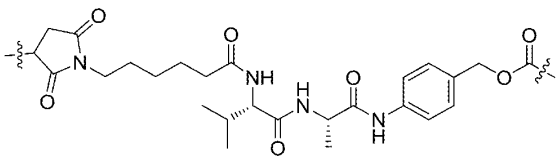

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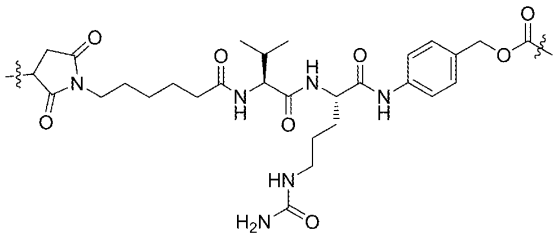

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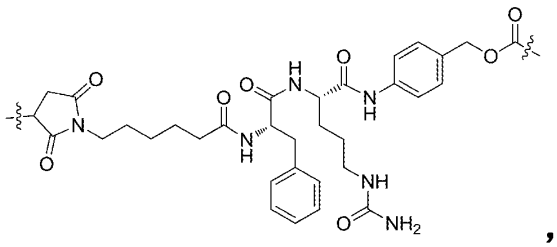

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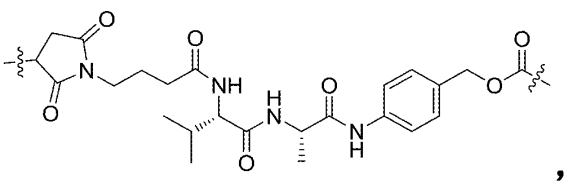

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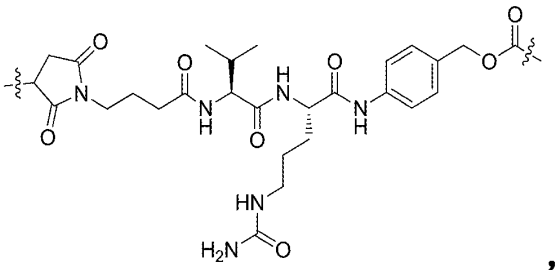

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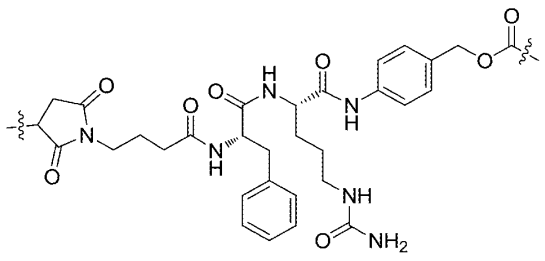
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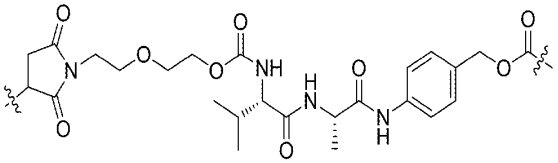
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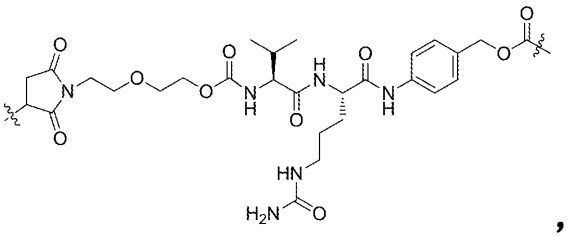
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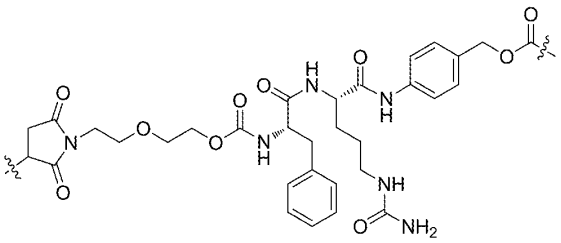
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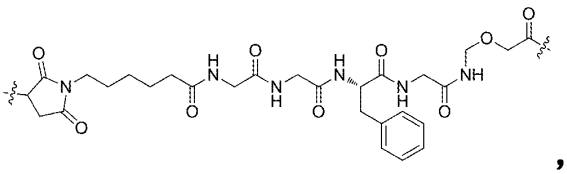
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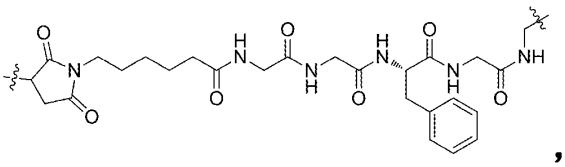
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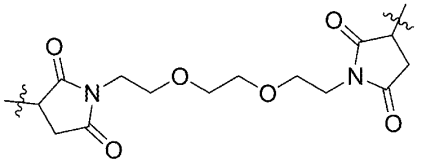
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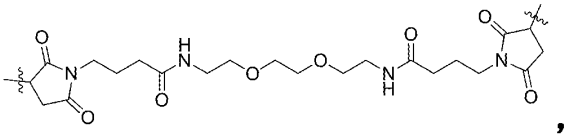
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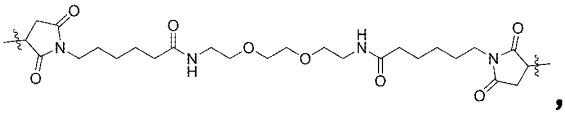
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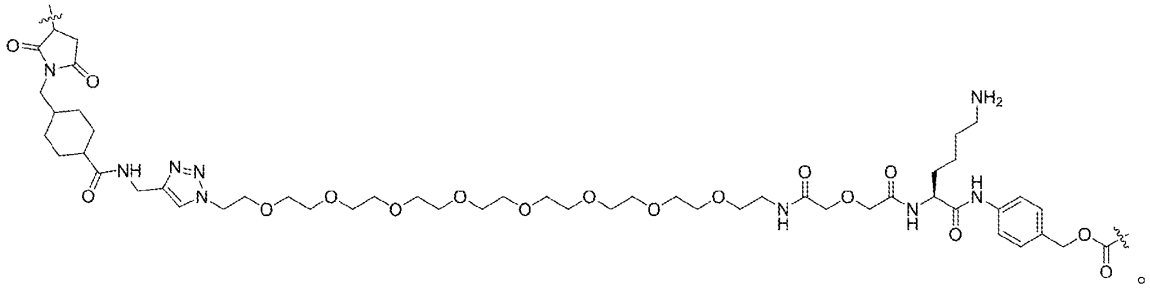
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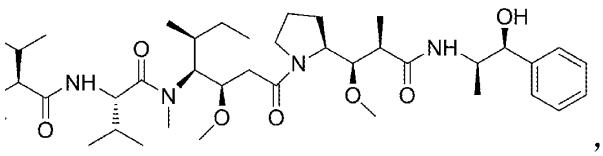


10.根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于：所述的抗体或其功能性结合片段包括单克隆抗体、多克隆抗体、抗体片段、Fab、Fab '、Fab '-SH、F(ab ')2、Fv、单链 Fv(“scFv”)、双抗体、线性抗体、双特异性抗体、多特异性抗体、嵌合抗体、人源化抗体、全人抗体、或包含抗体的抗原结合部分的融合蛋白；优选的，所述的抗体为人源化单克隆抗体或全人抗体。

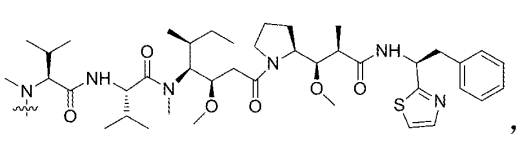
11.根据权利要求 10 所述的抗体药物偶联物，其特征在于：所述的抗体为 IgG 抗体或其功能性结合片段，进一步优选的，所述的抗体为 IgG_1、IgG_2、IgG_3、IgG_4。

12.根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于：所述的活性药物单元为细胞毒分子、细胞分化因子、干细胞营养因子、类固醇类药物、治疗自身免疫疾病的药物、抗炎症药物或治疗传染性疾病的药物。

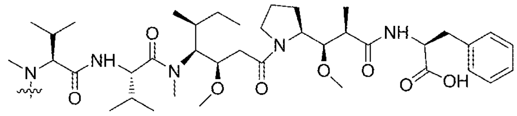
13.根据权利要求 12 所述的抗体药物偶联物，其特征在于：所述细胞毒分子包括但不限于微管蛋白抑制剂或 DNA 损伤剂；进一步优选的，所述微管蛋白抑制剂包括但不限于海兔毒素(dolastatin)及奥瑞他汀(auristatin)类细胞毒分子，美登素（maytansine）类细胞毒分子；所述 DNA 损伤剂包括但不限于卡奇霉素类（calicheamicin）、倍癌霉素（duocarmycin）类、安曲霉素类衍生物 PBD、喜树碱(camptothecins)及喜树碱类衍生物、SN-38；进一步优选的，所述奥瑞他汀（auristatin）类细胞素分子包括但不限于 MMAE 或 MMAF 或它们的衍生物，所述美登素类细胞毒分子包括但不限于 DM1、DM4 或它们的衍生物；进一步优选的，所述细胞毒分子包括以下结构：

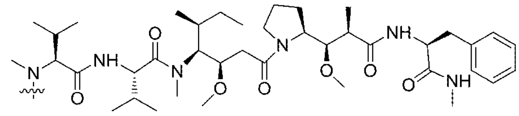


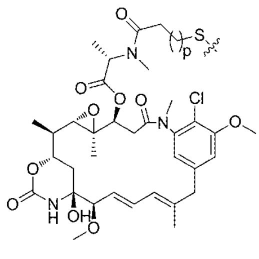
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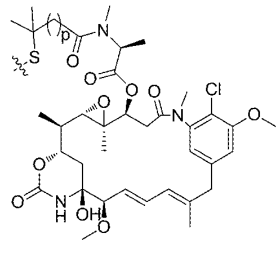


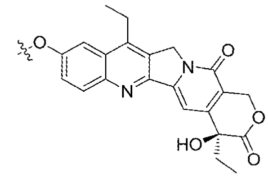
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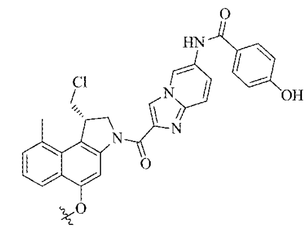

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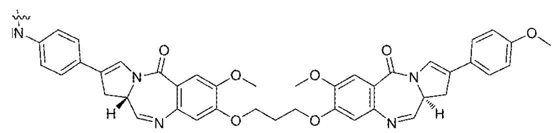

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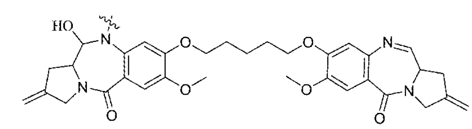

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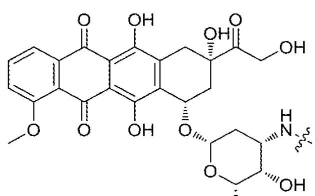

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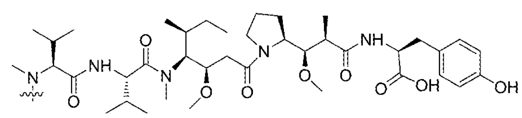

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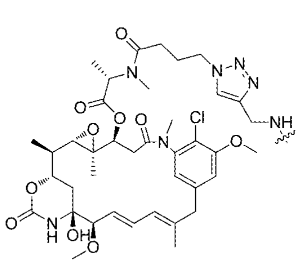

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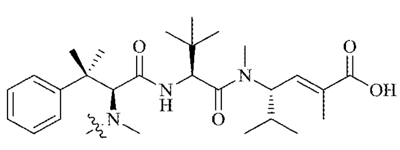

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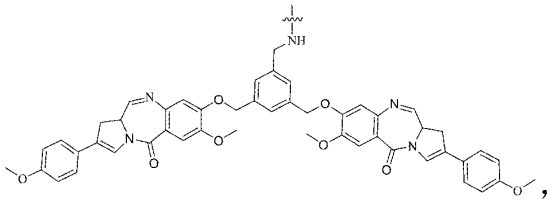
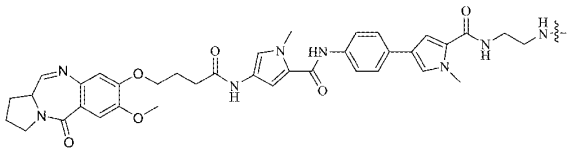
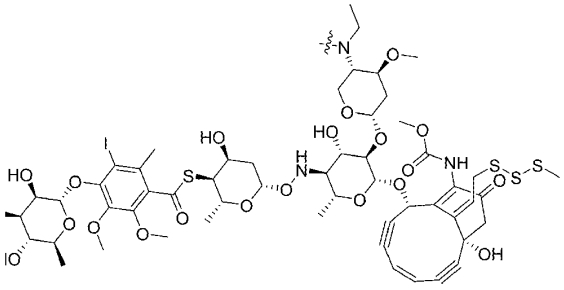
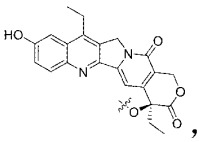
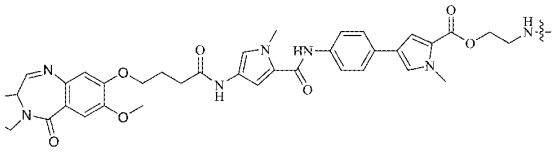
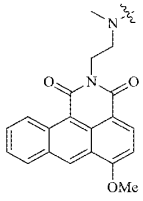
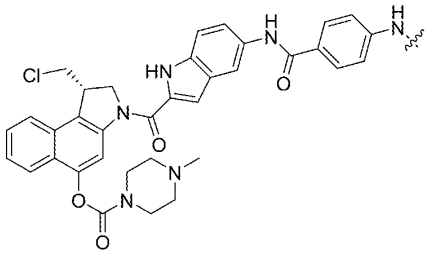
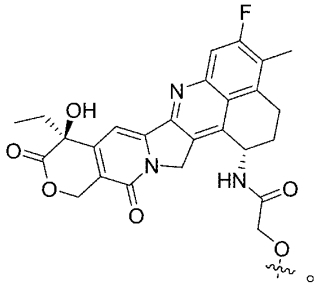

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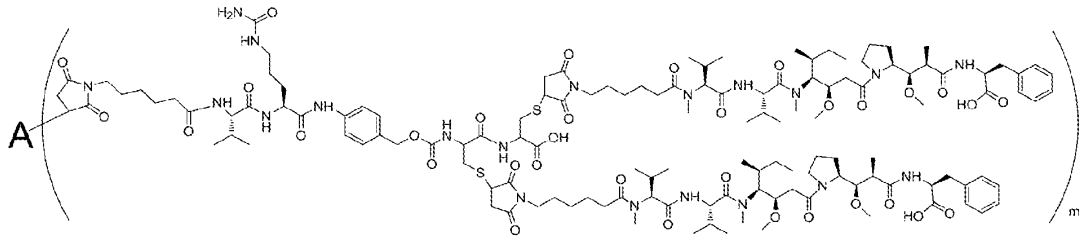

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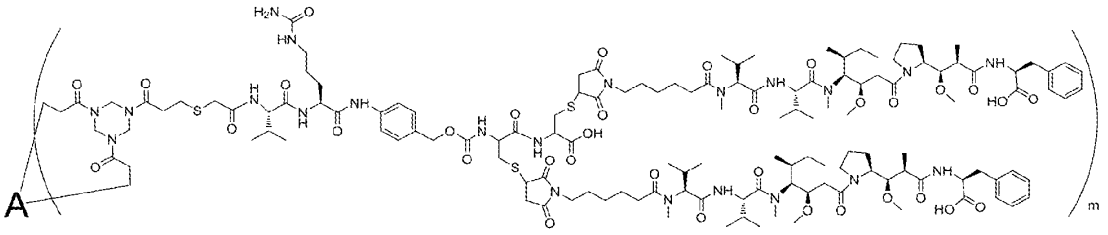

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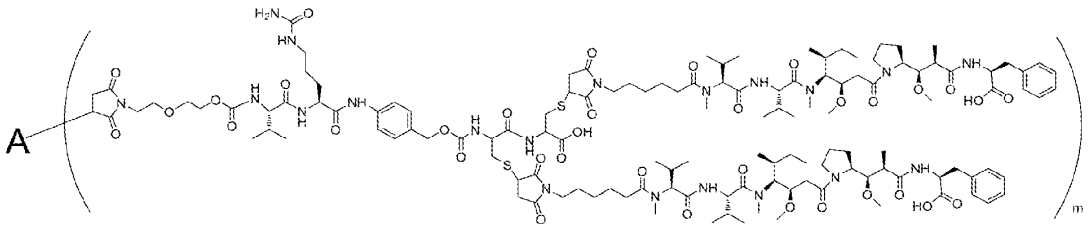

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14.根据以上权利要求任意一项所述的抗体药物偶联物，其特征在于：所述抗体药物偶联物结构如下所示：

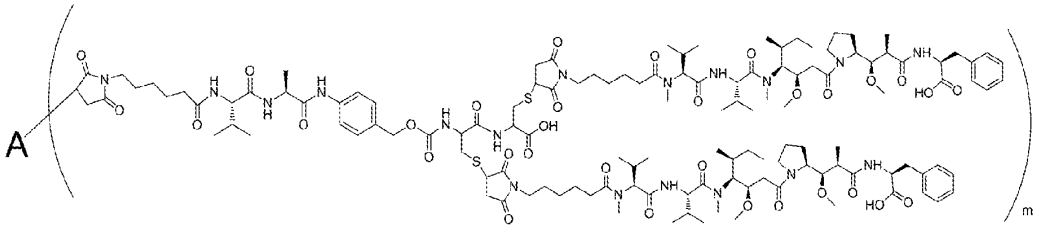

ADC-1



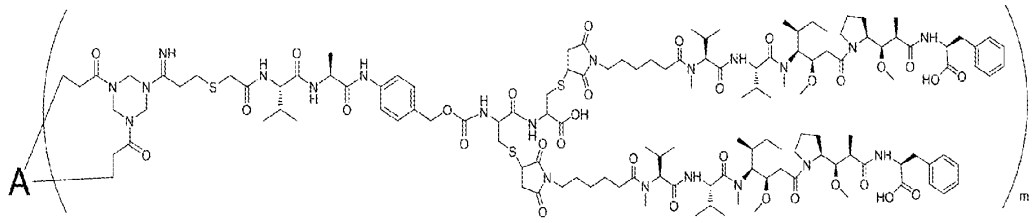
ADC-2



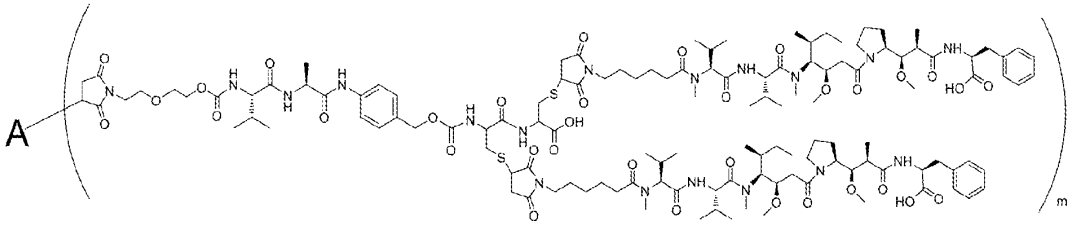
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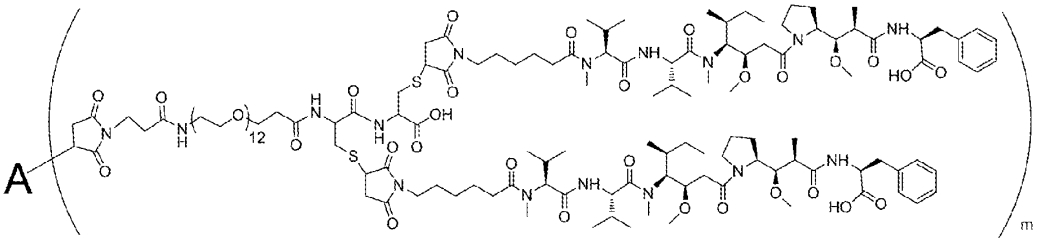
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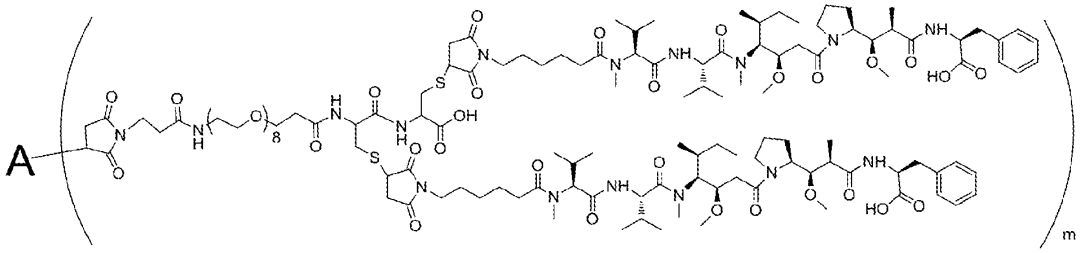
ADC-5



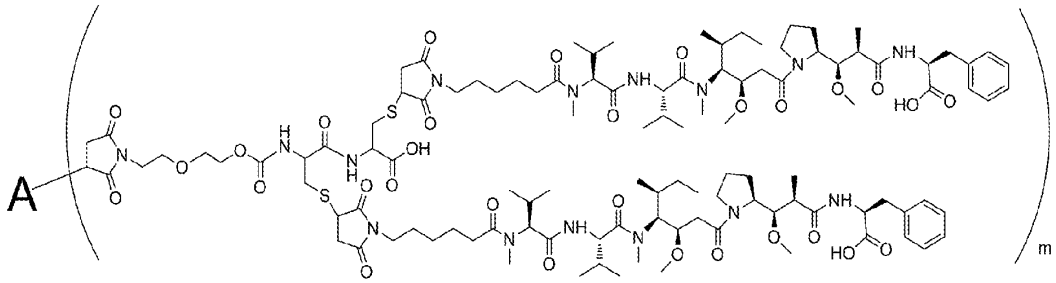
ADC-6



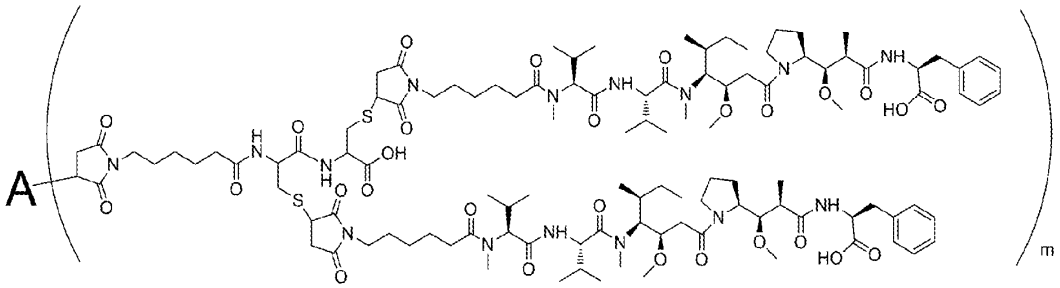
ADC-7



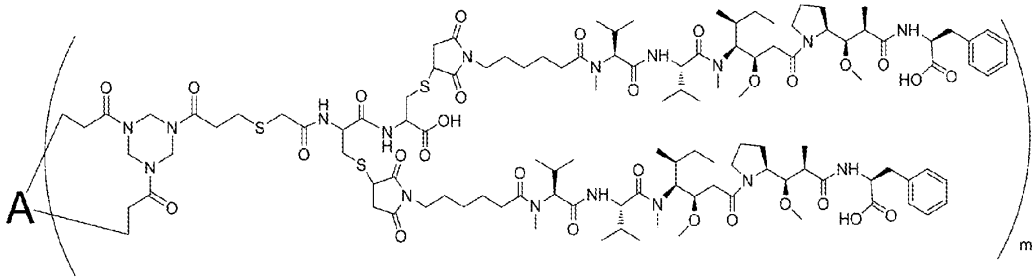
ADC-8



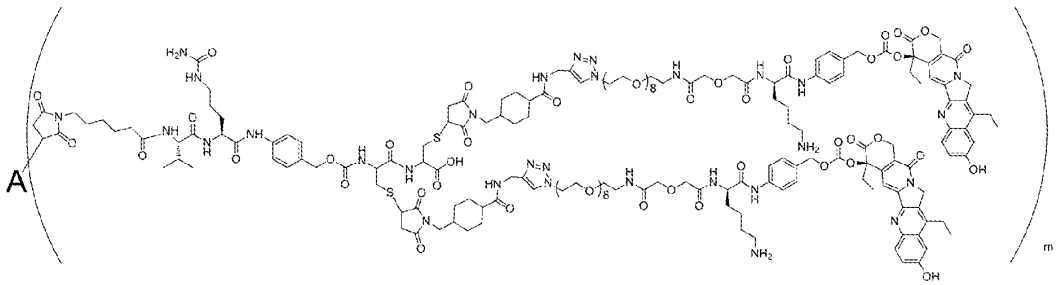
ADC-9



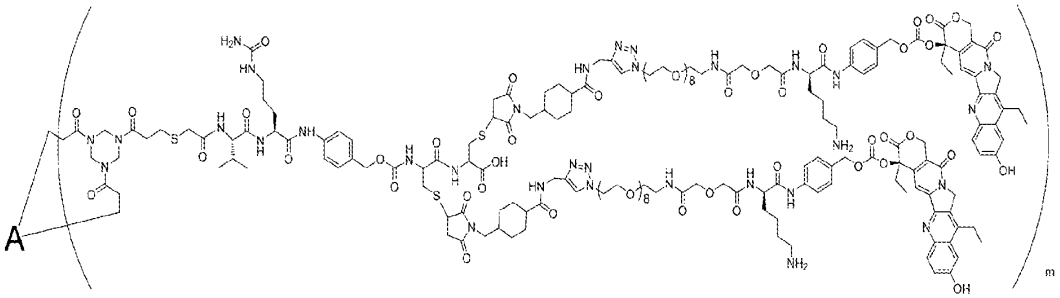
ADC-10



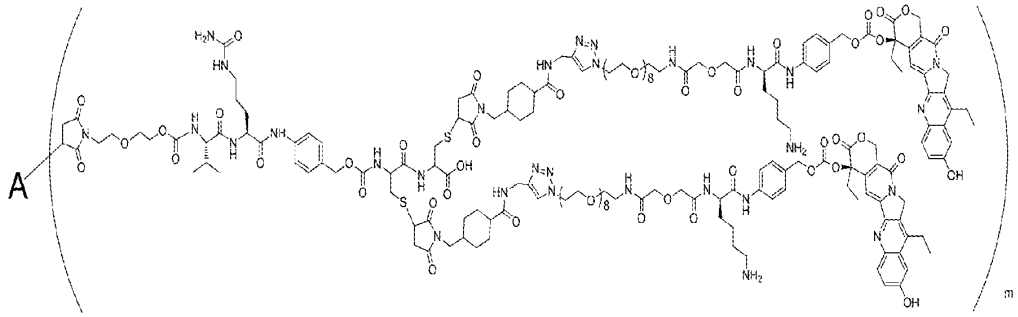
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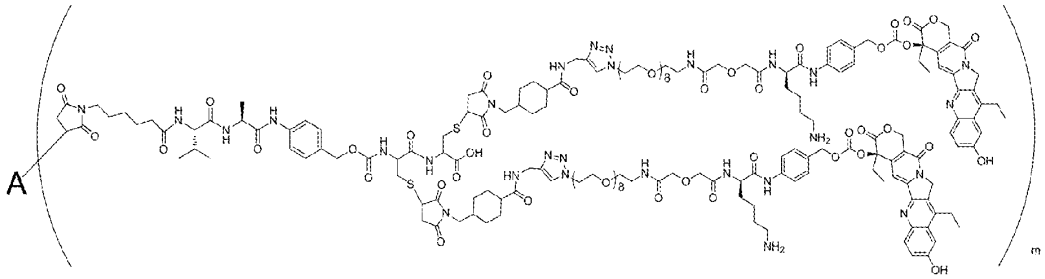
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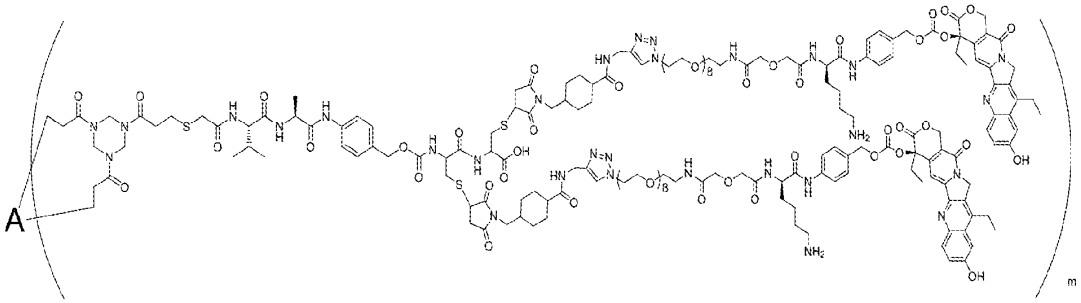
ADC-13



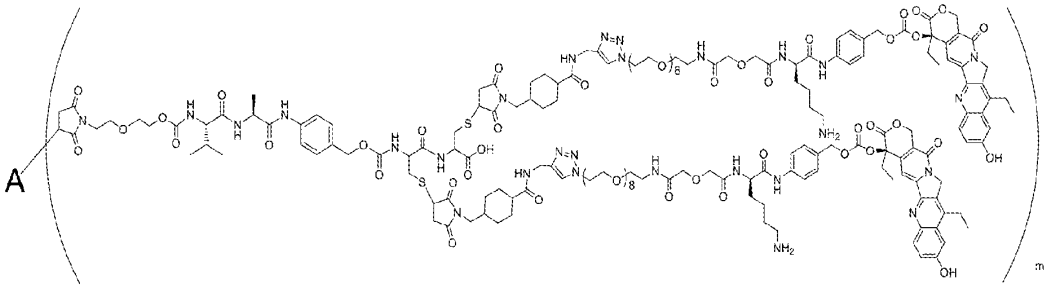
ADC-14



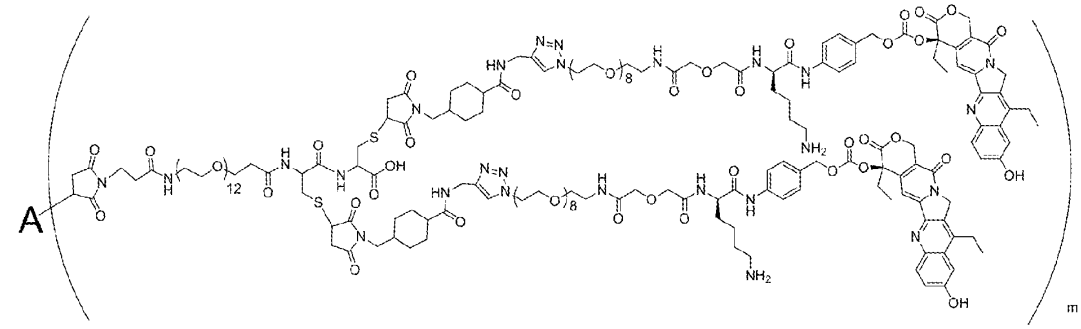
ADC-15



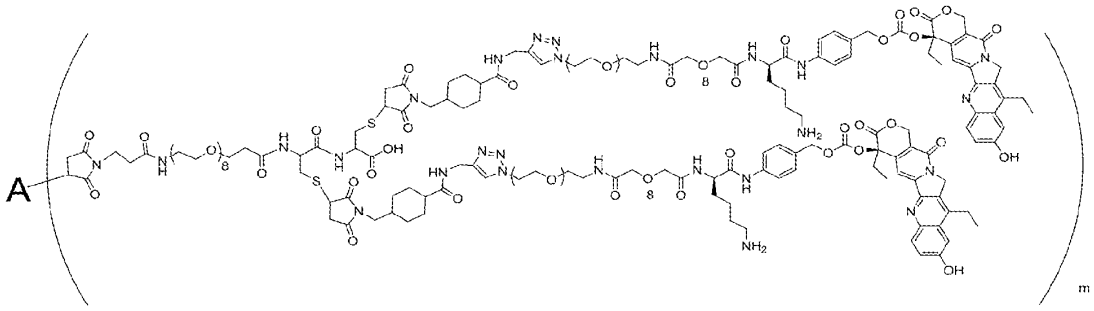
ADC-16



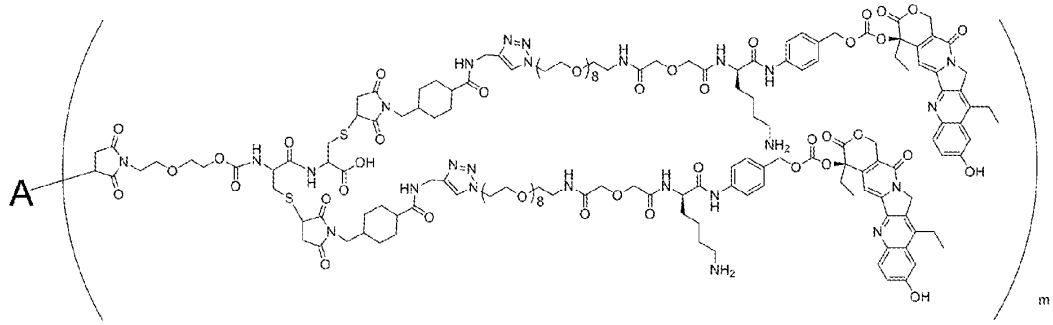
ADC-17



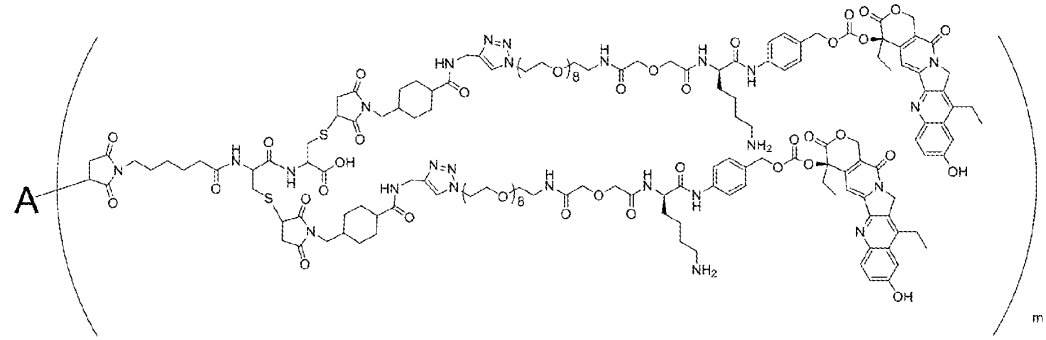
ADC-18



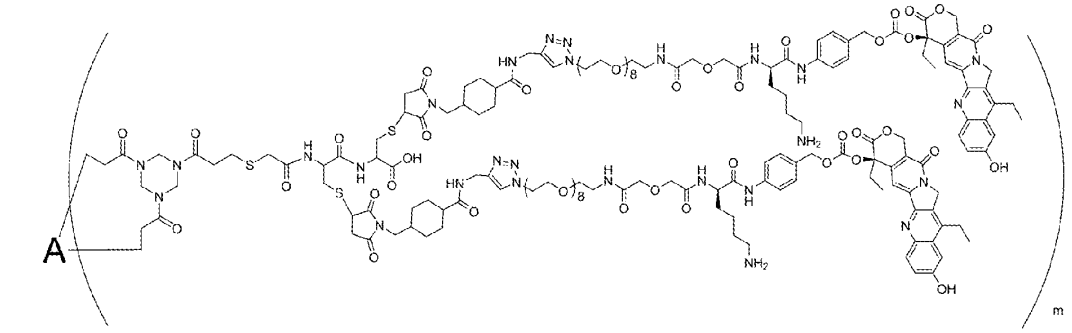
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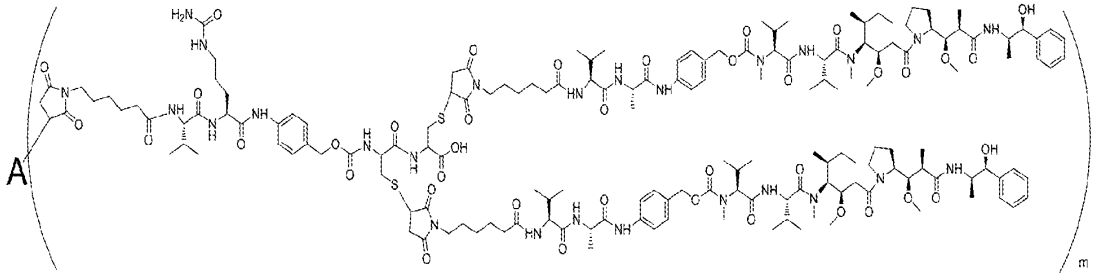
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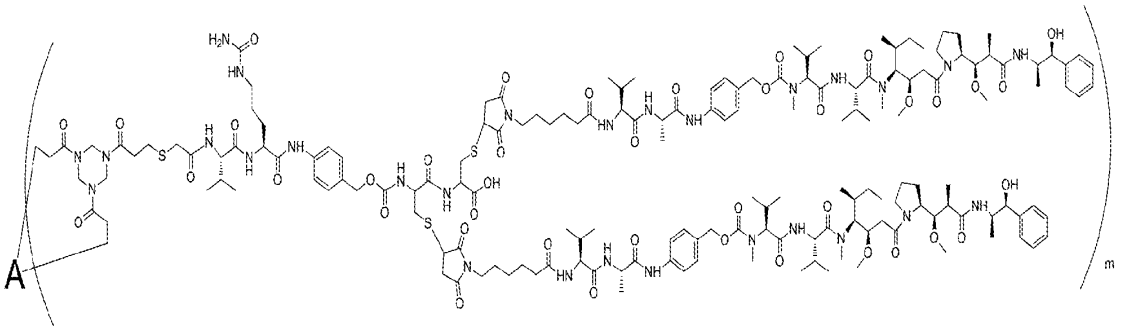
ADC-21



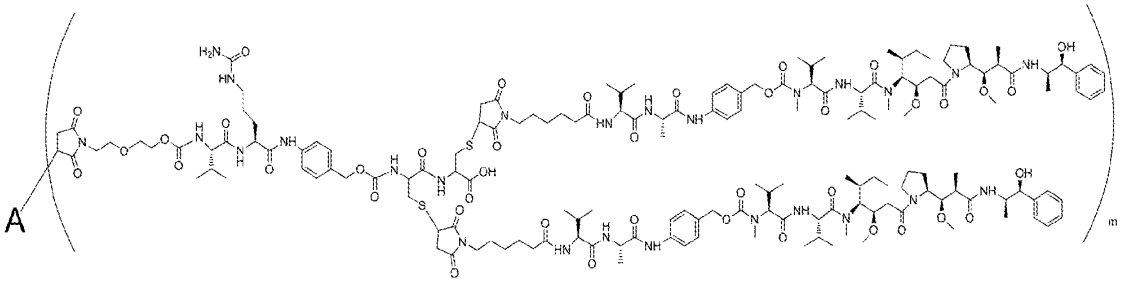
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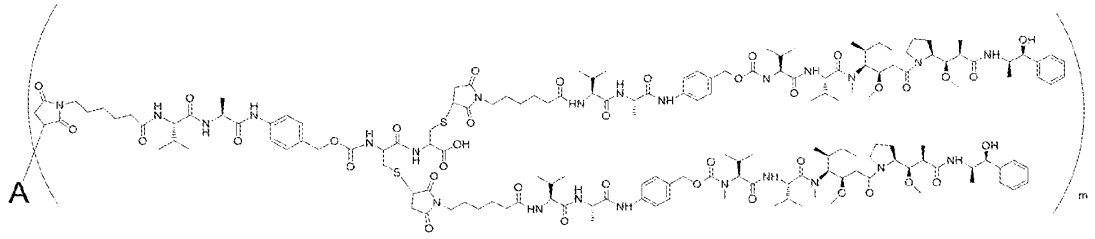
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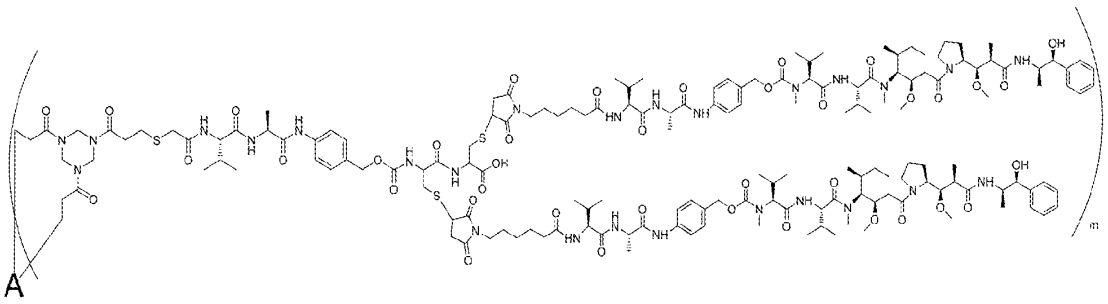
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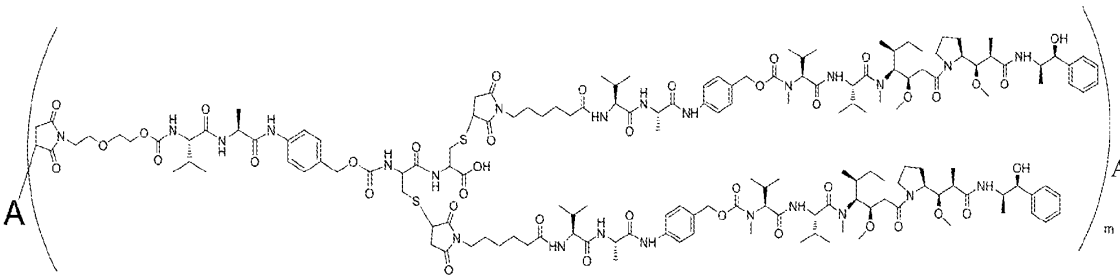
ADC-25



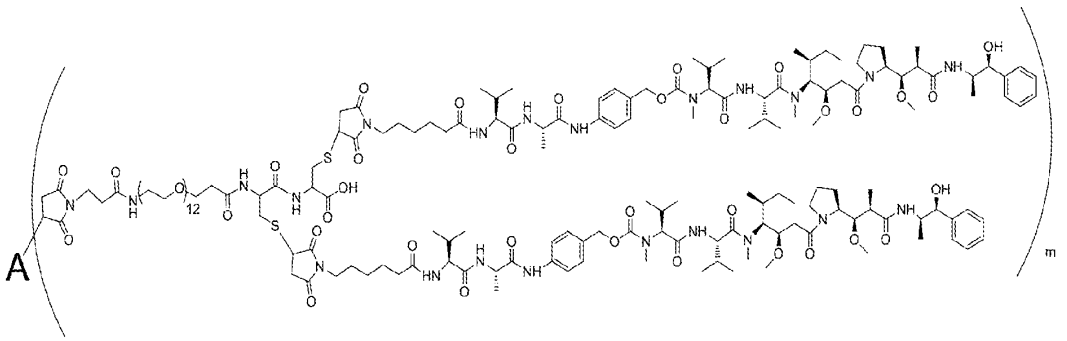
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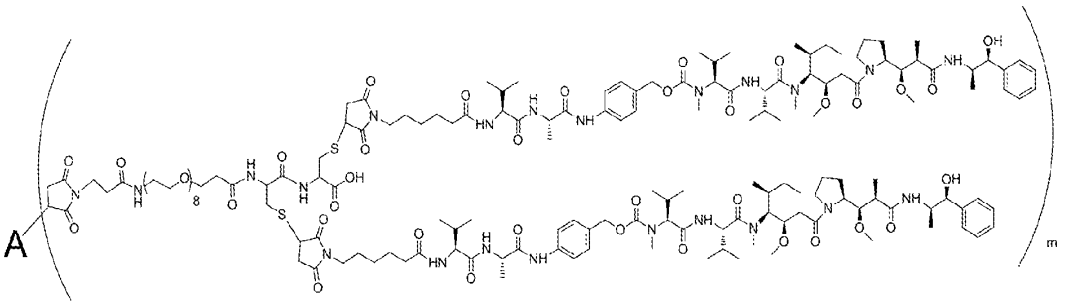
ADC-27



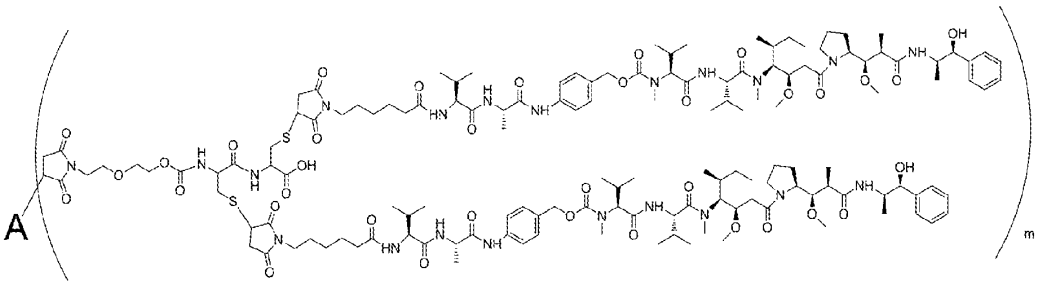
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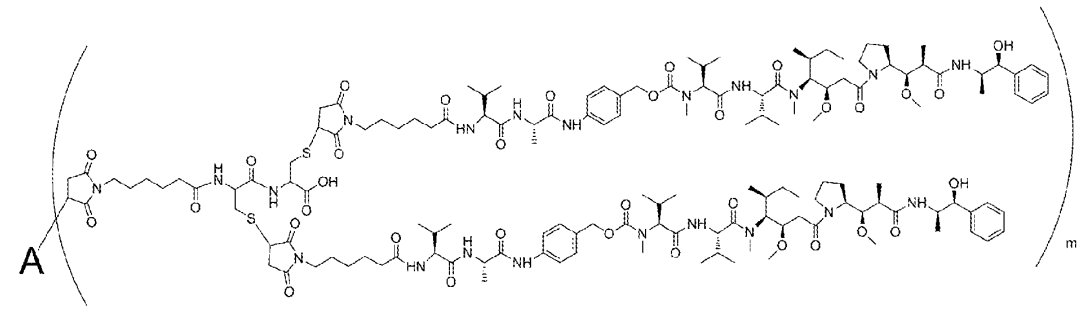
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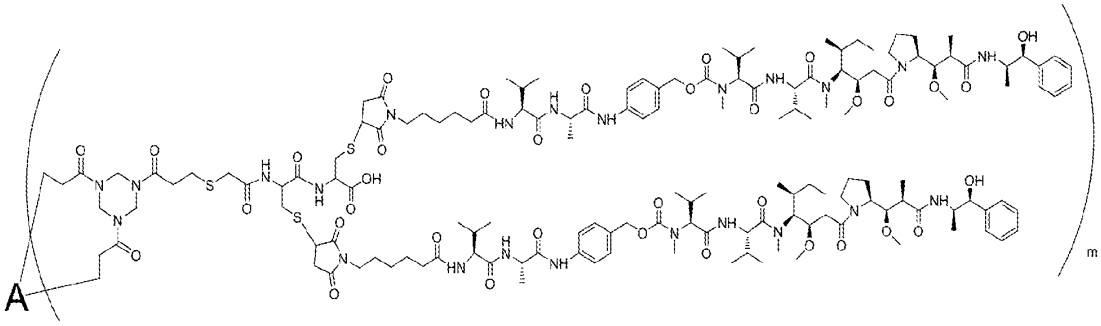
ADC-30



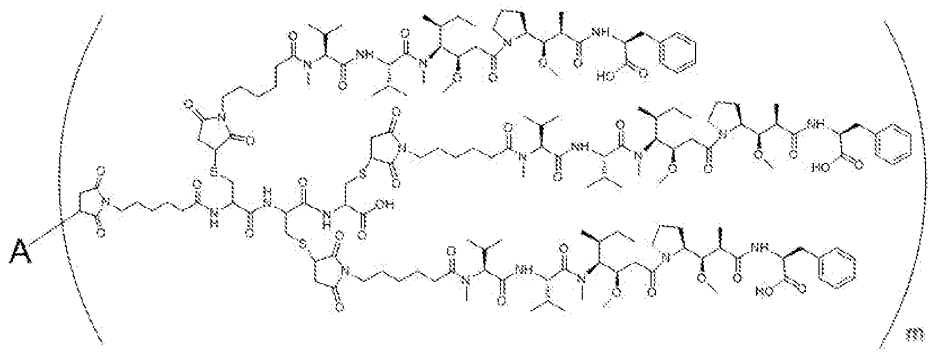
ADC-31



ADC-32



ADC-33



ADC-34

其中：

A 为任一抗体或其功能性结合片段；

m 选自 1、2、3、4、5、6、7、8。

15. 一种药物组合物，包含有效量的权利要求 1-14 中任一项所述抗体药物偶联物或其药学上可接受的盐或溶剂合物，以及药学上可接受的辅料。

16. 权利要求 1-14 中任一项所述的抗体药物偶联物在制备治疗癌症药物中的用途。