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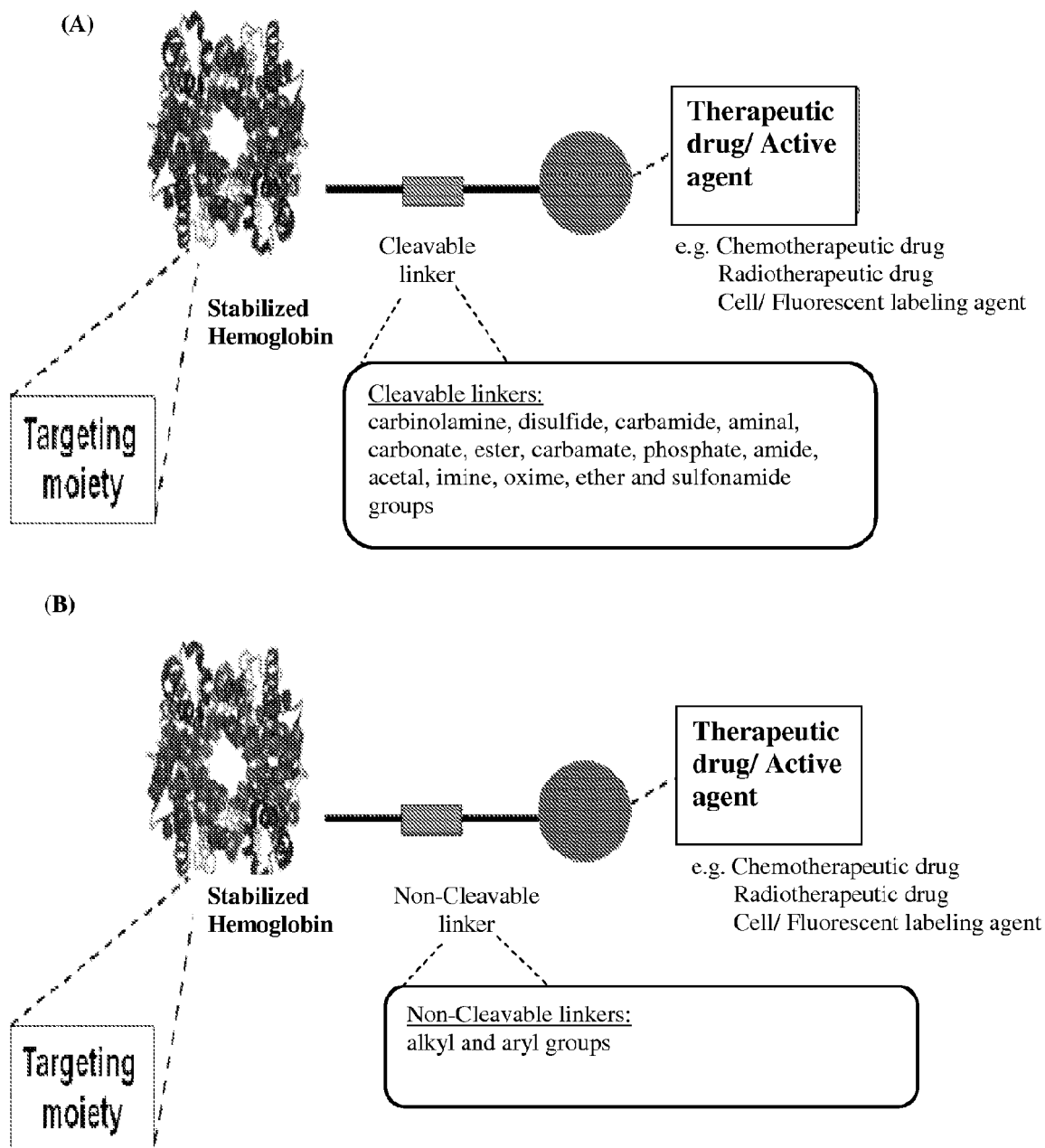


FIG. 1

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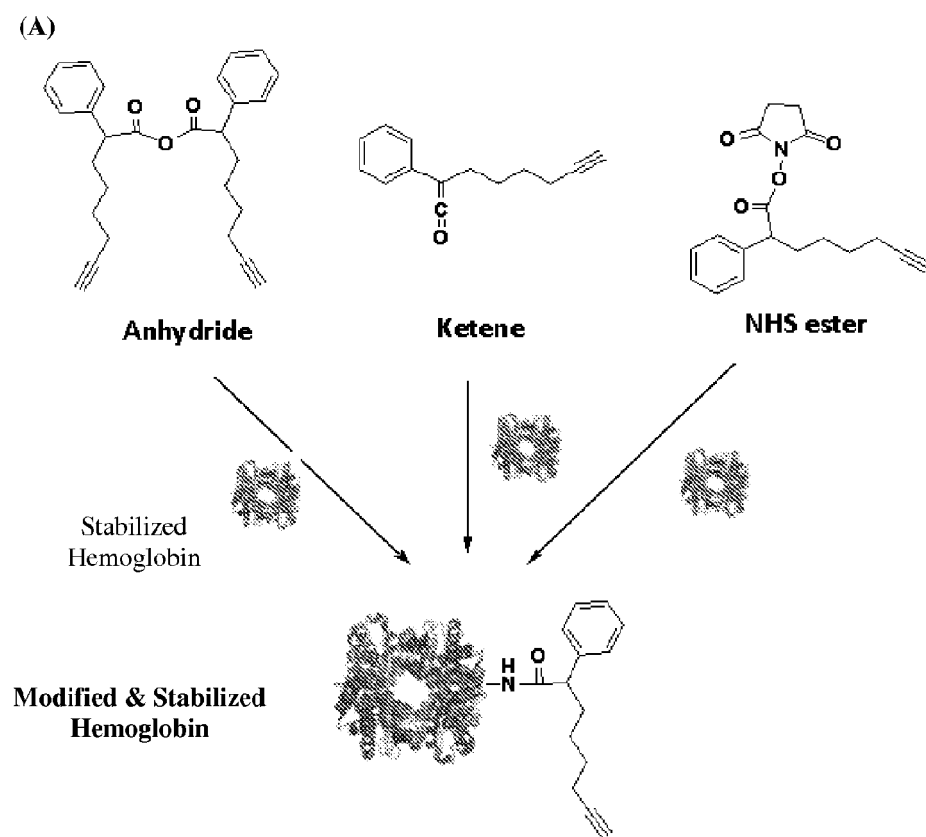


FIG. 3

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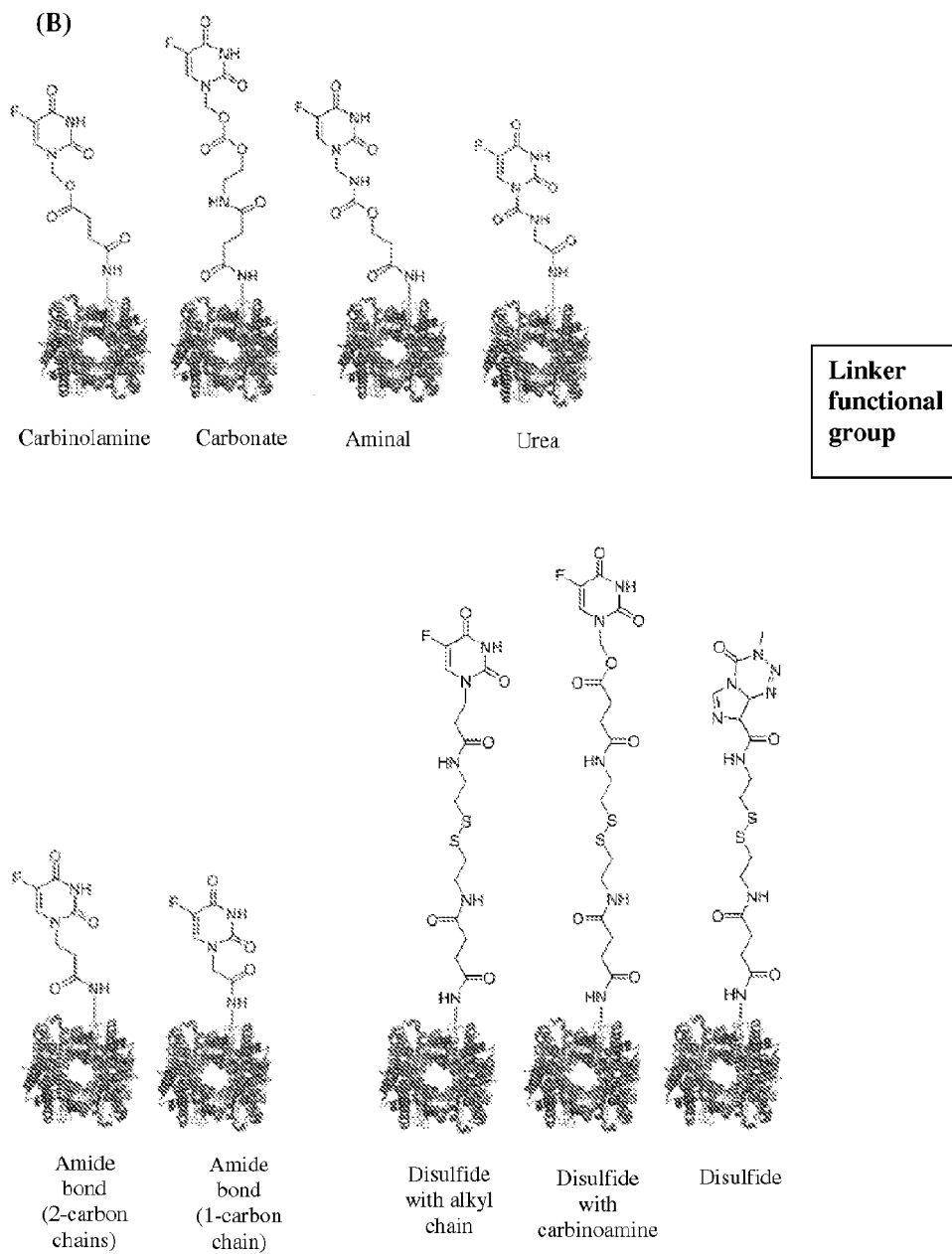


FIG. 3 (cont'd)

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(A)

Non-cleavable Scheme

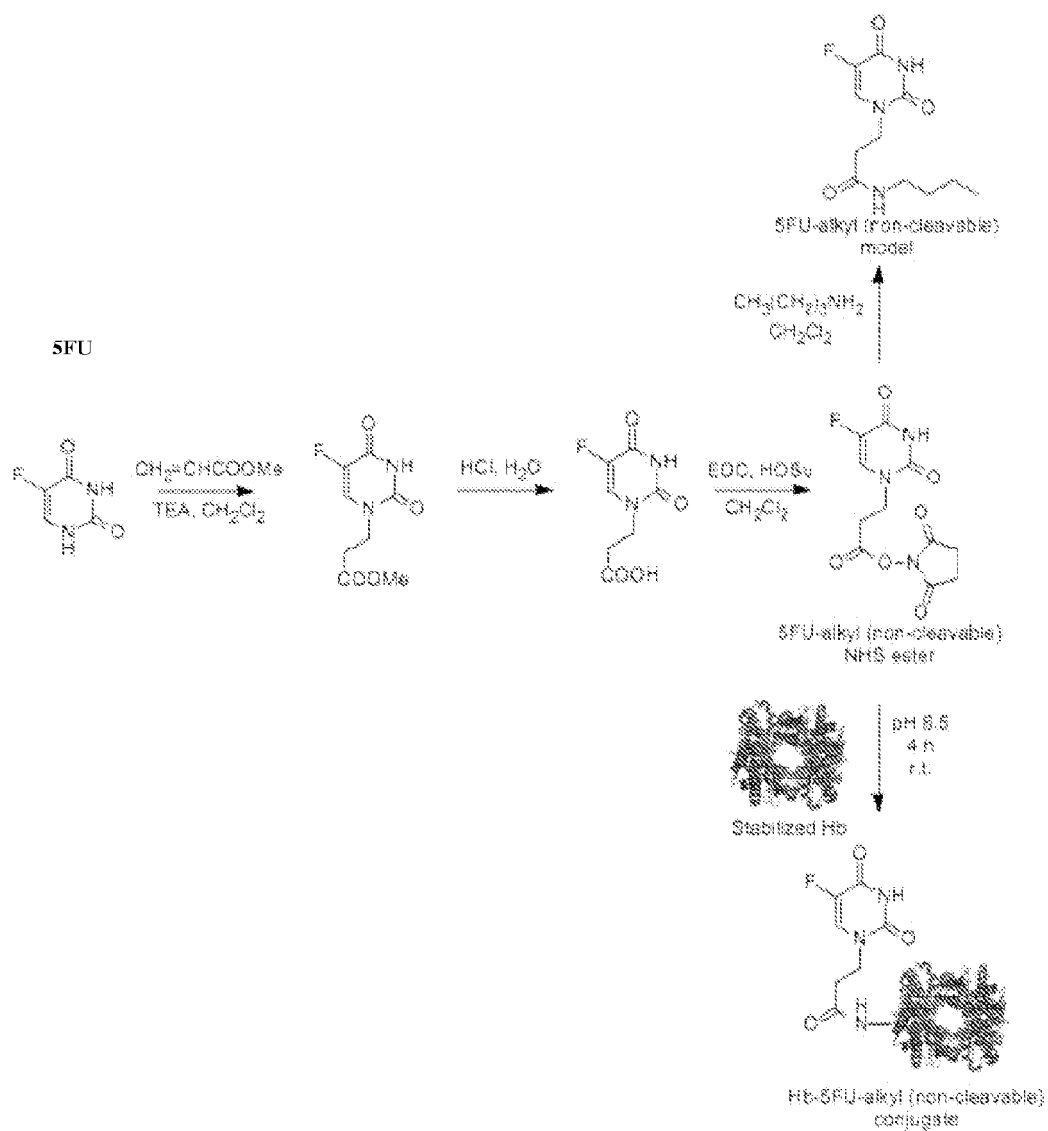
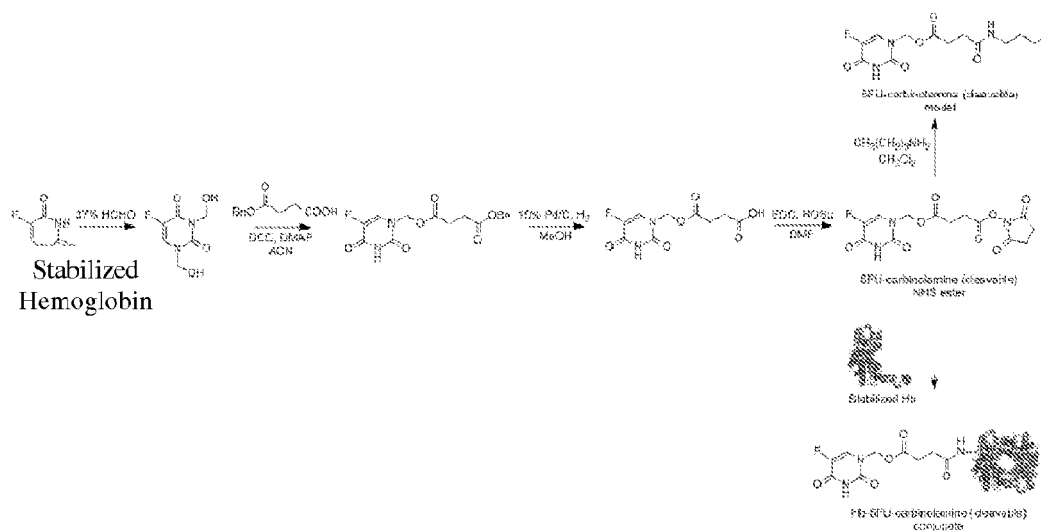


FIG. 4

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Cleavable Scheme

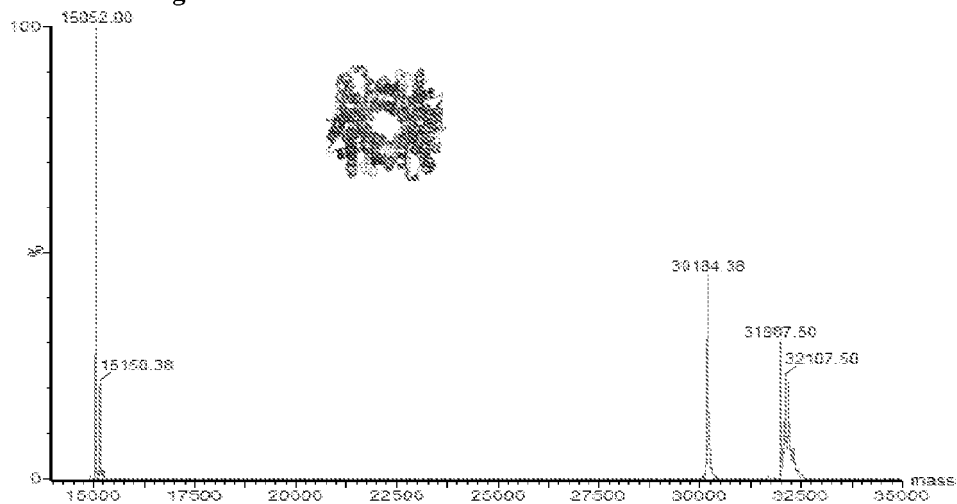
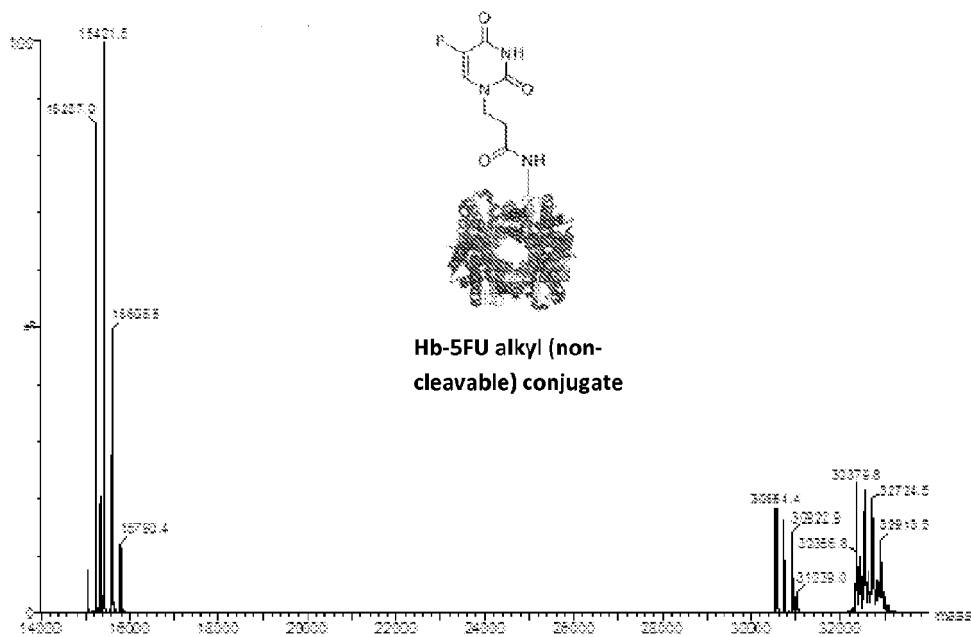
(B)



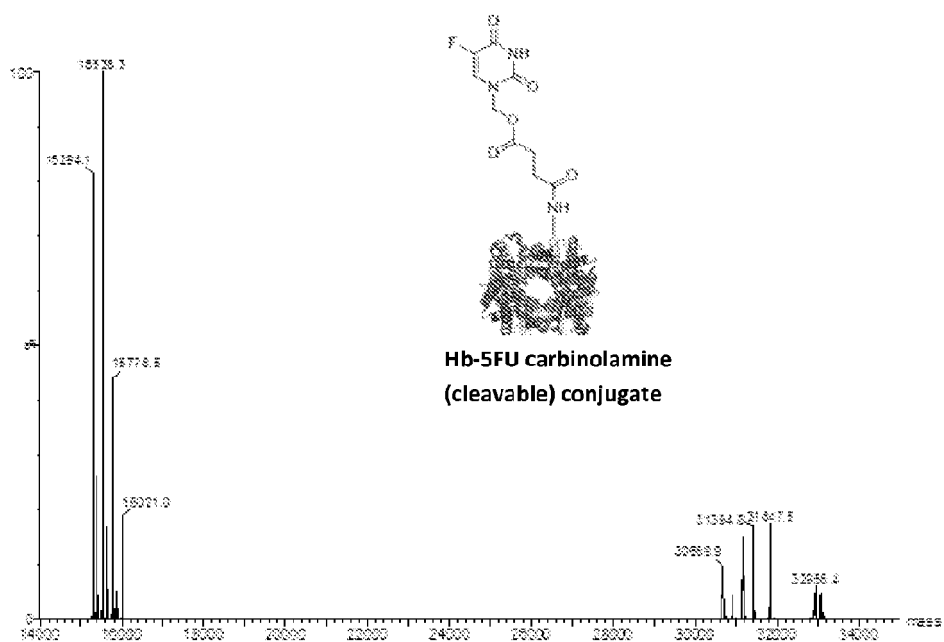
Hemoglobin-based 5FU

FIG. 4 (cont'd)

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(A) Stabilized Hemoglobin**(B) Hemoglobin-based 5FU (non-cleavable conjugate)****FIG. 5**

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(C) Hemoglobin-based 5FU (cleavable conjugate)

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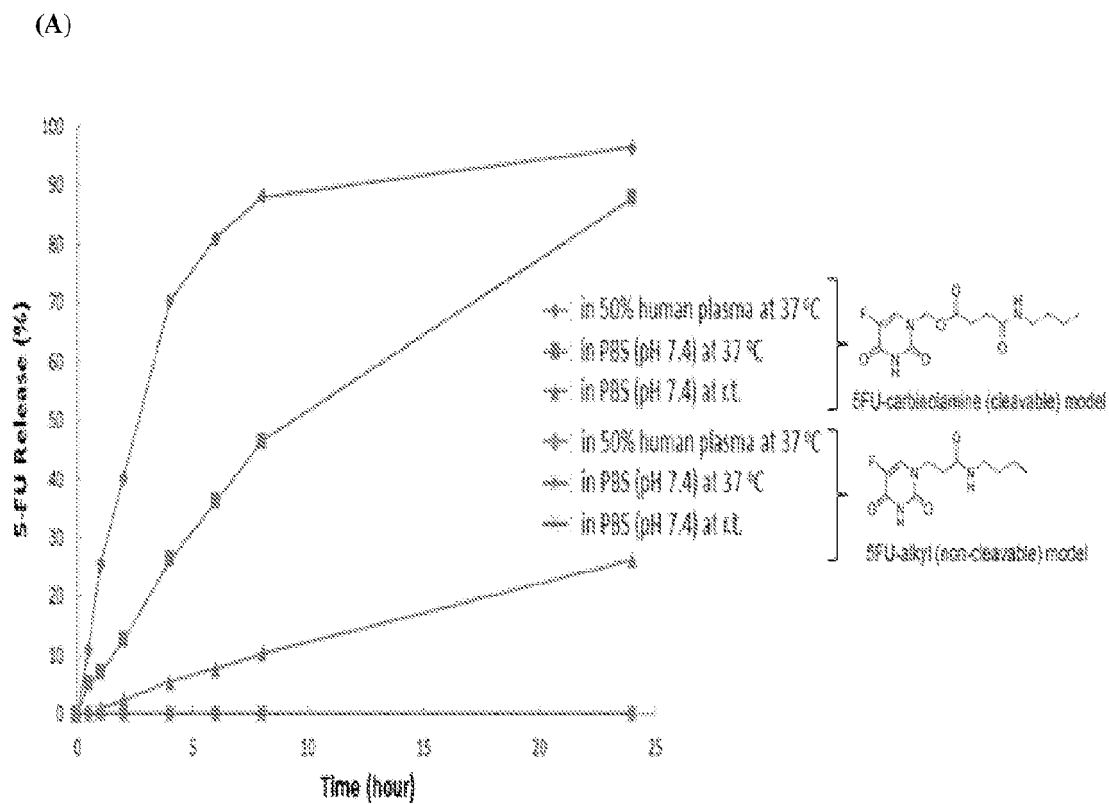


FIG. 6

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(B)

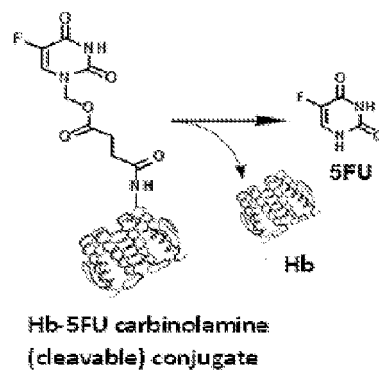
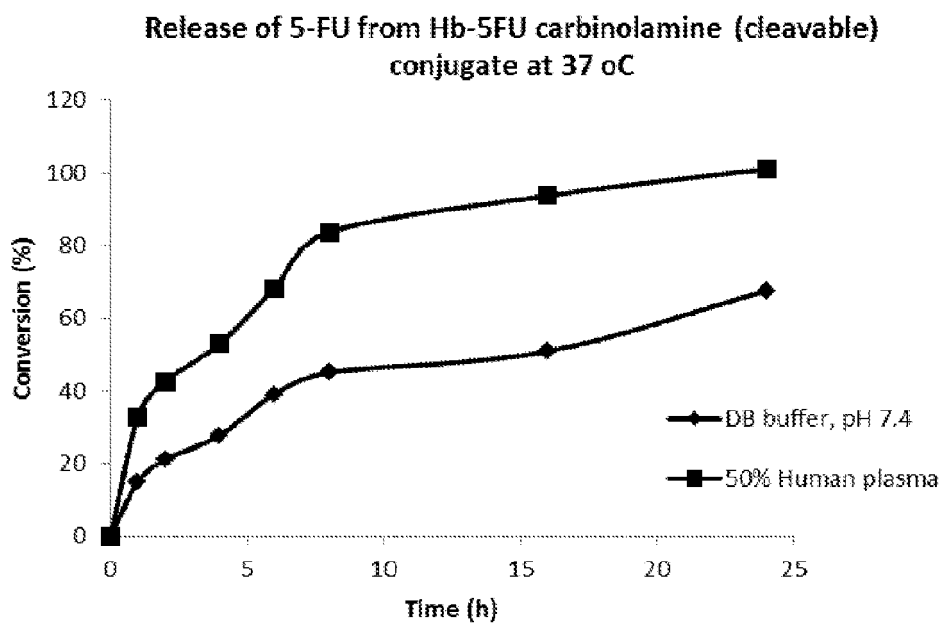
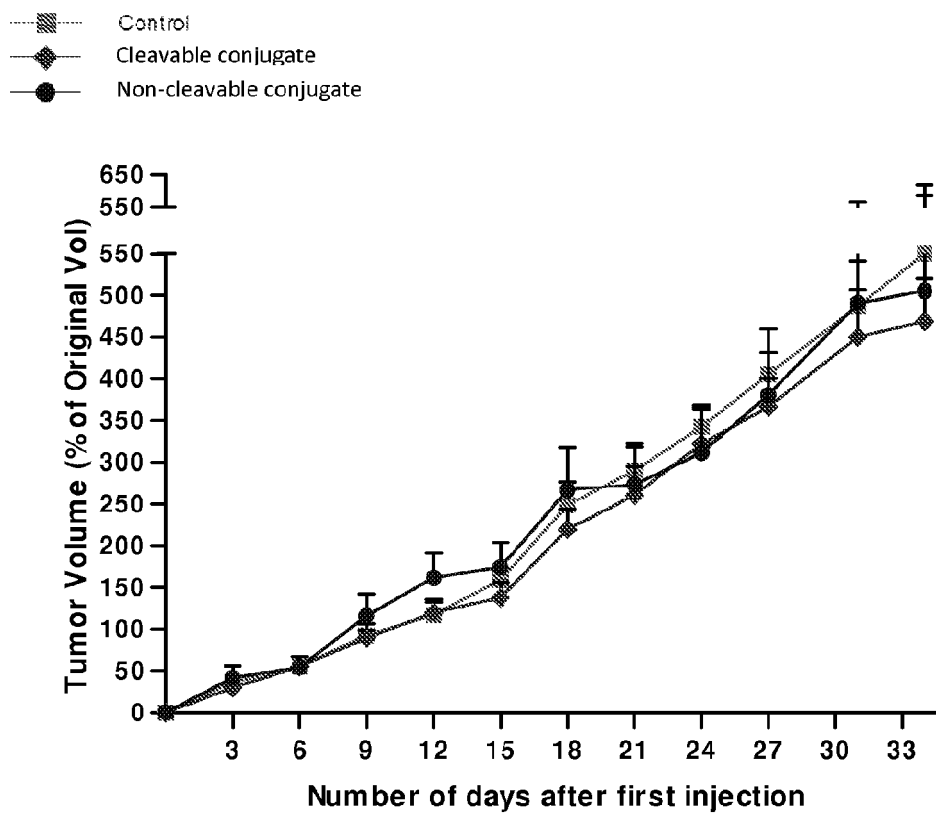


FIG. 6 (cont'd)

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Tumor growth in pancreatic cancer Capan-1 xenograft nude mice model

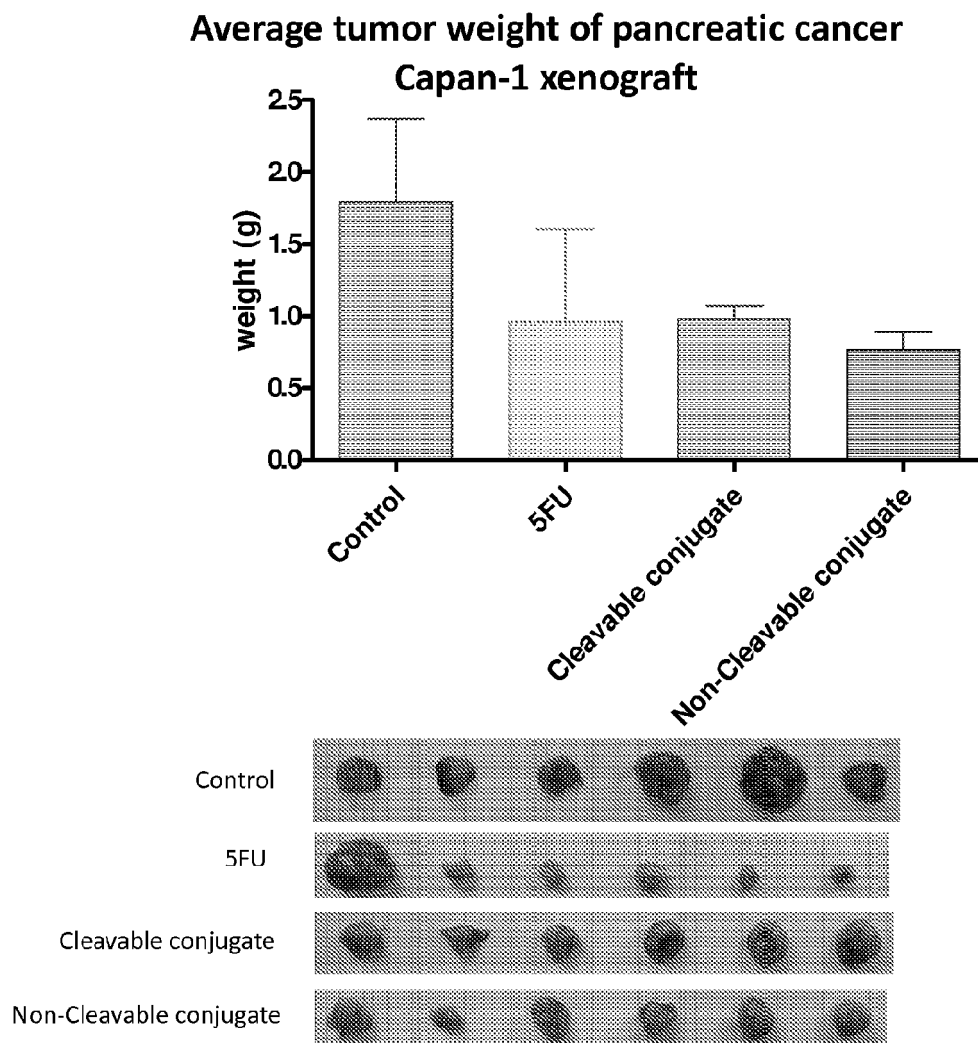


Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 7

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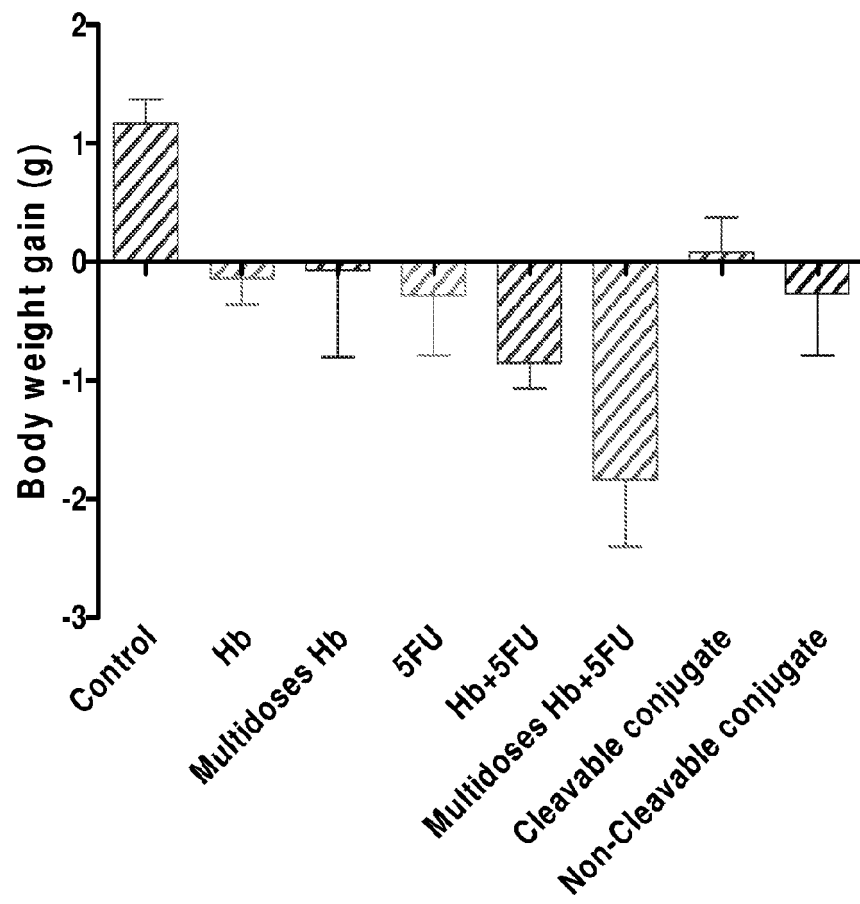
Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 8

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**Weight change of mice carrying pancreatic cancer
Capan-1 xenograft after drug treatment**



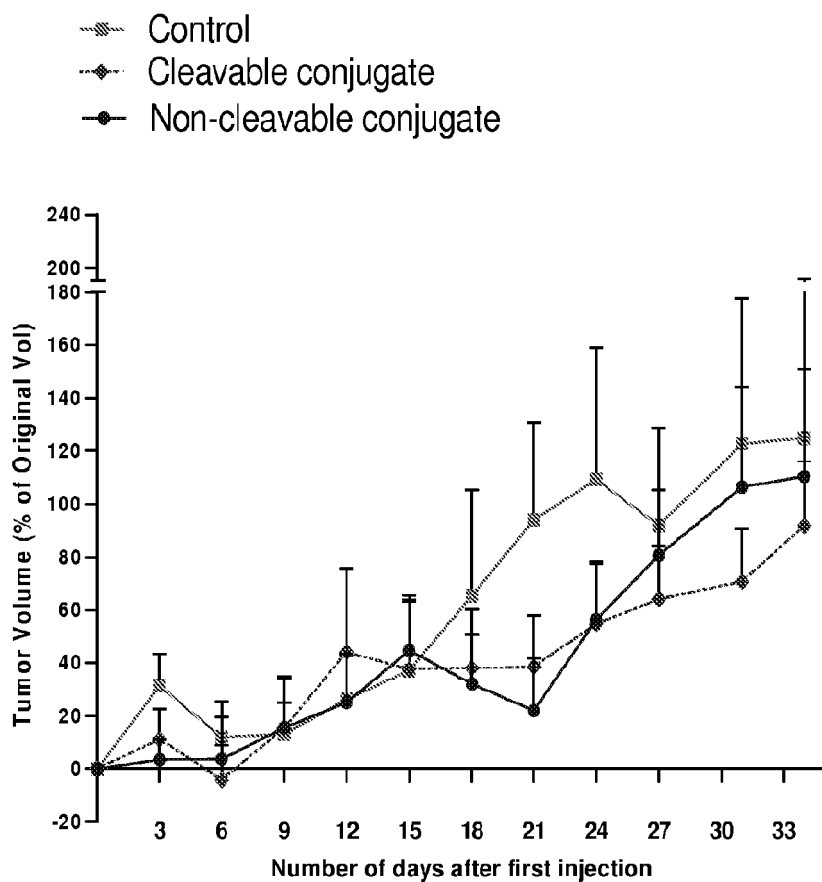
Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 9

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Tumor growth in liver cancer SMMC7221 xenograft nude mice model

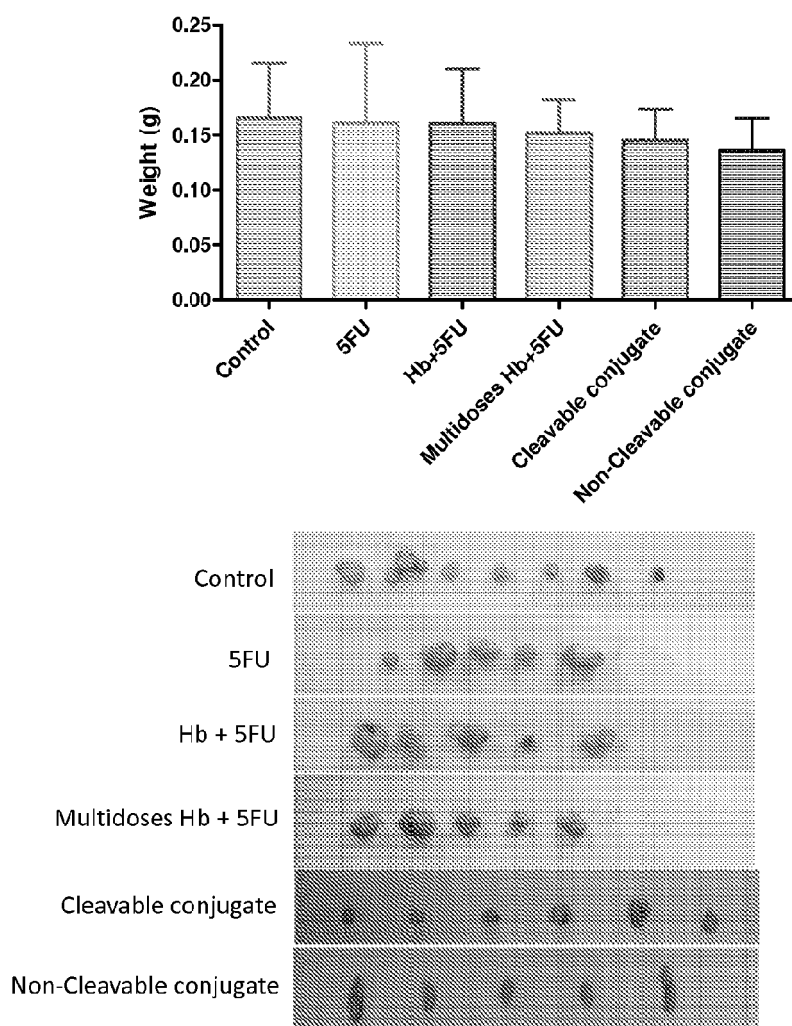


Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 10

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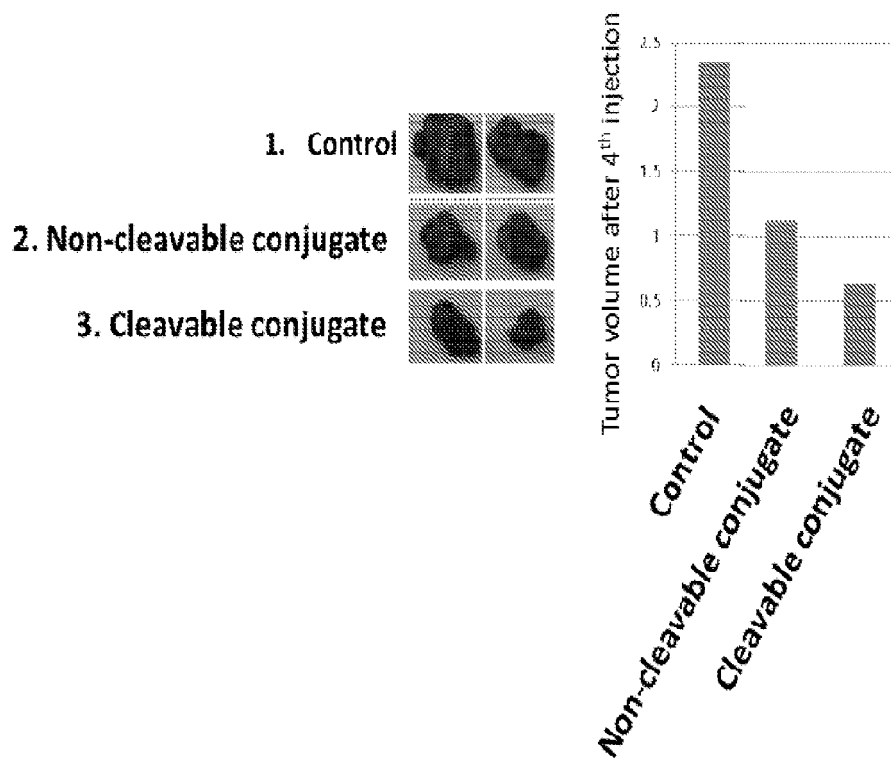
Average tumor weight of liver cancer SMMC7721 xenograft

Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 11

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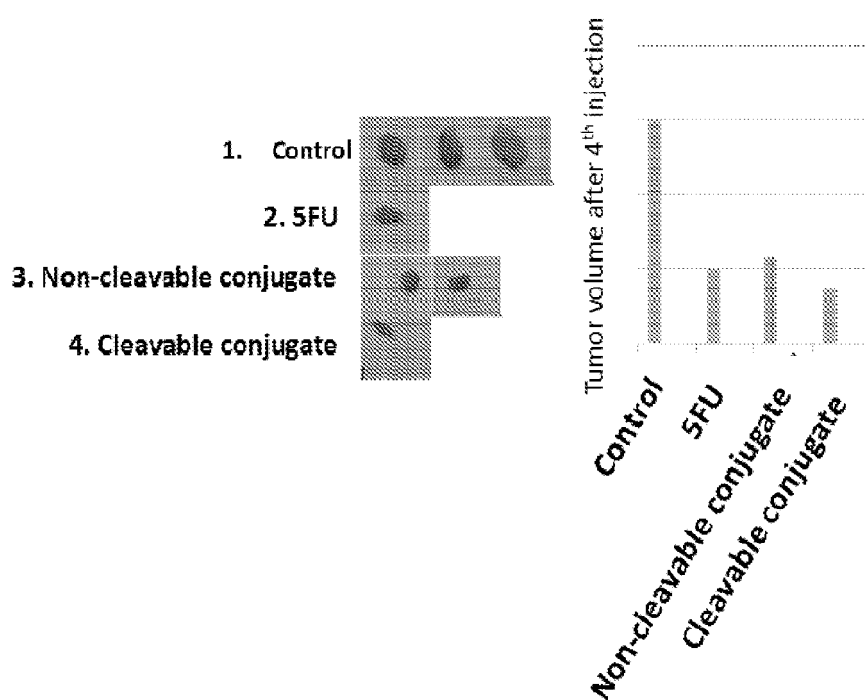
Tumor growth of CD133+ Liver cancer stem cell animal model (HepG2)

Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 12

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Tumor growth of CD44+CD24- Breast cancer stem cell animal model (MCF7)

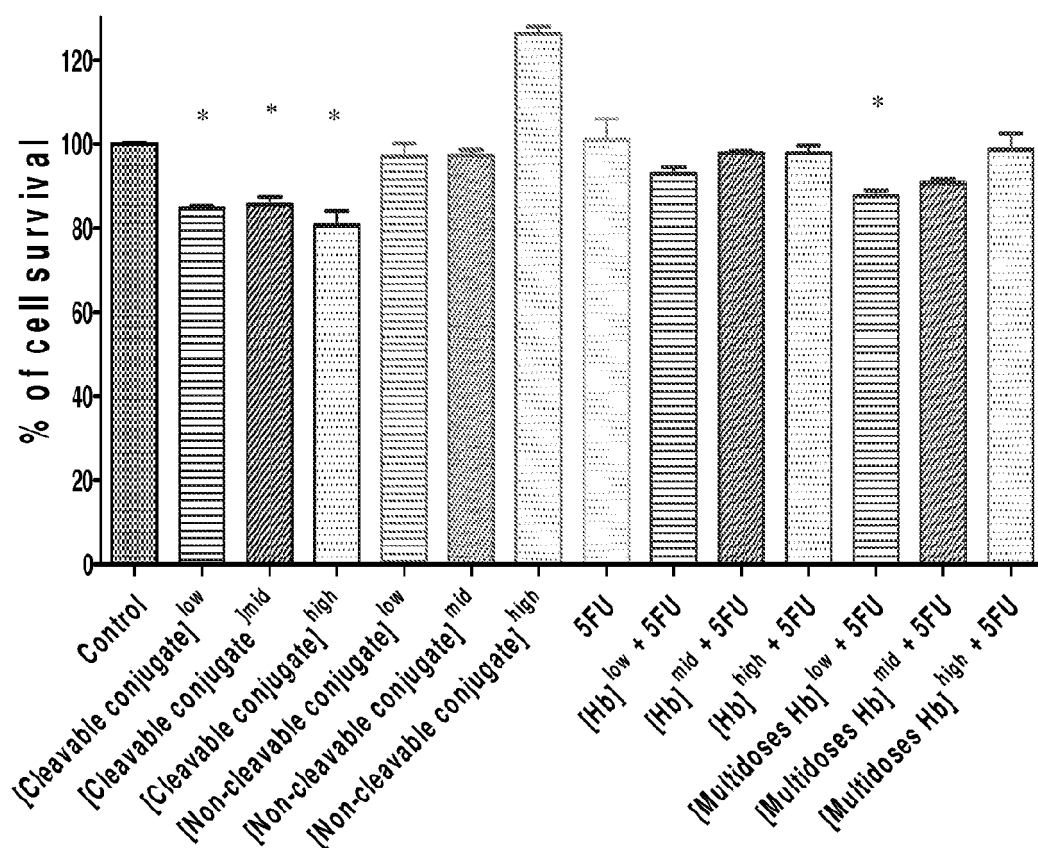
Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 13

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MTT Assay – Colon cancer cell line HCT116



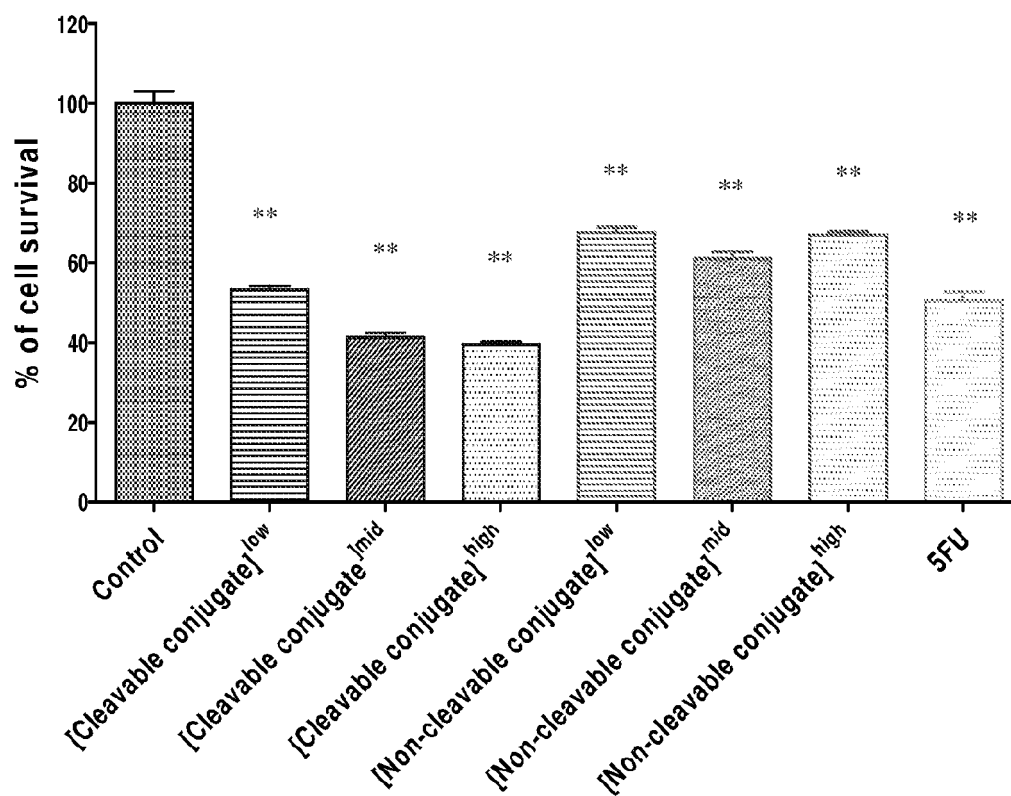
*, $p < 0.05$ compare to control

Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 14

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MTT Assay – Lung cancer cell line H460

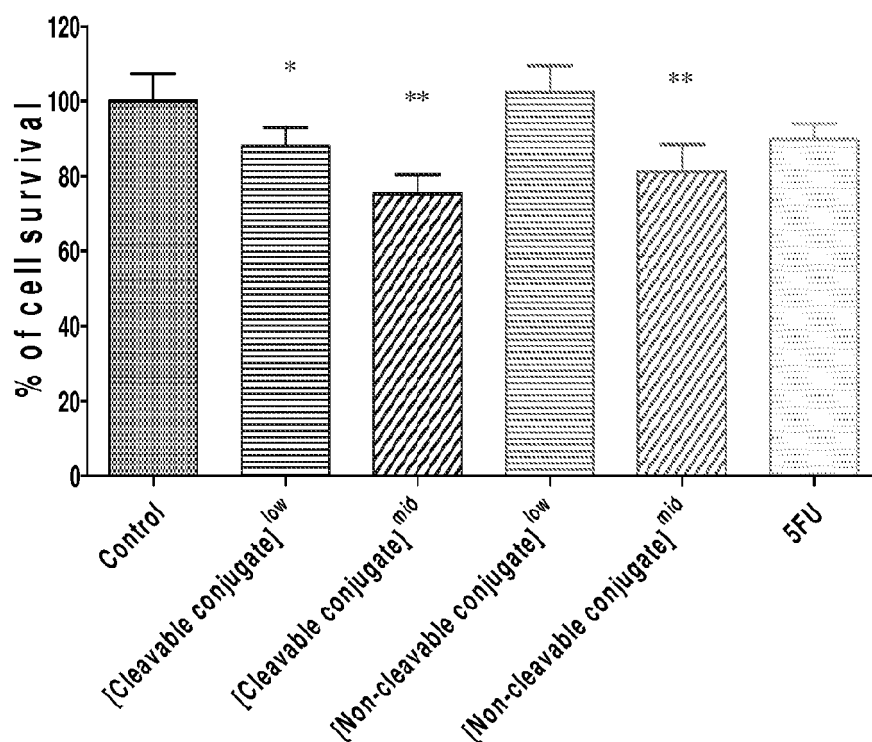
**, $p < 0.001$ compare to control

Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 15

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MTT Assay – Leukemia cell line Jurkat (Normoxic)

*, $p < 0.05$ compare to control; **, $p < 0.001$ compare to control

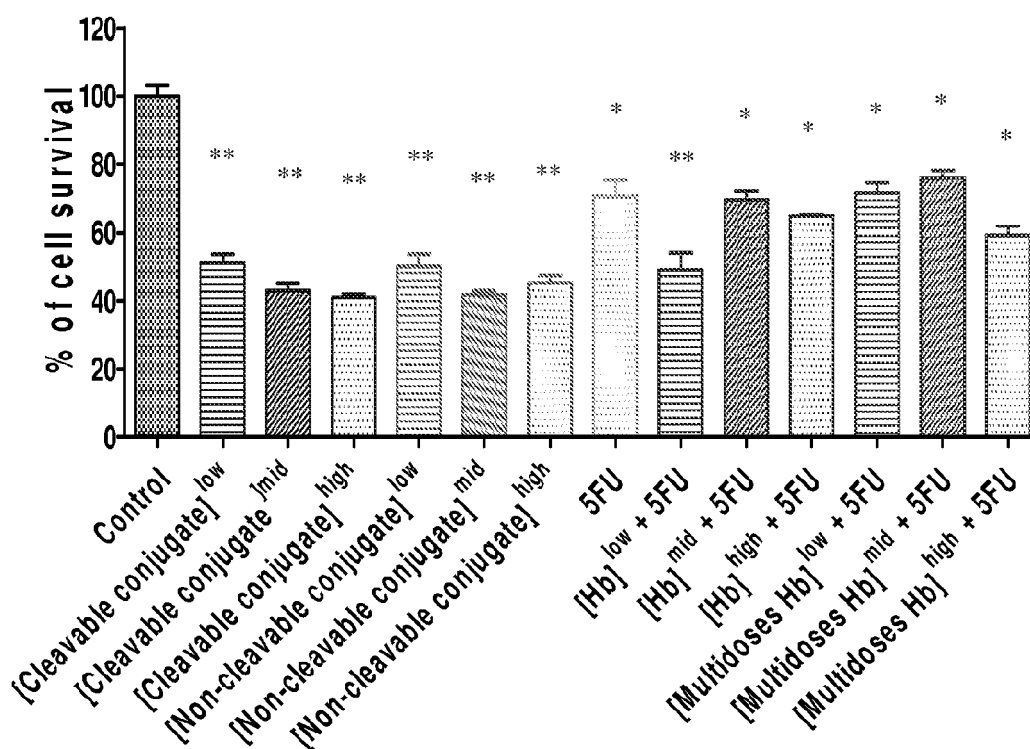
Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 16

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MTT Assay – Brain Cancer cell line A172



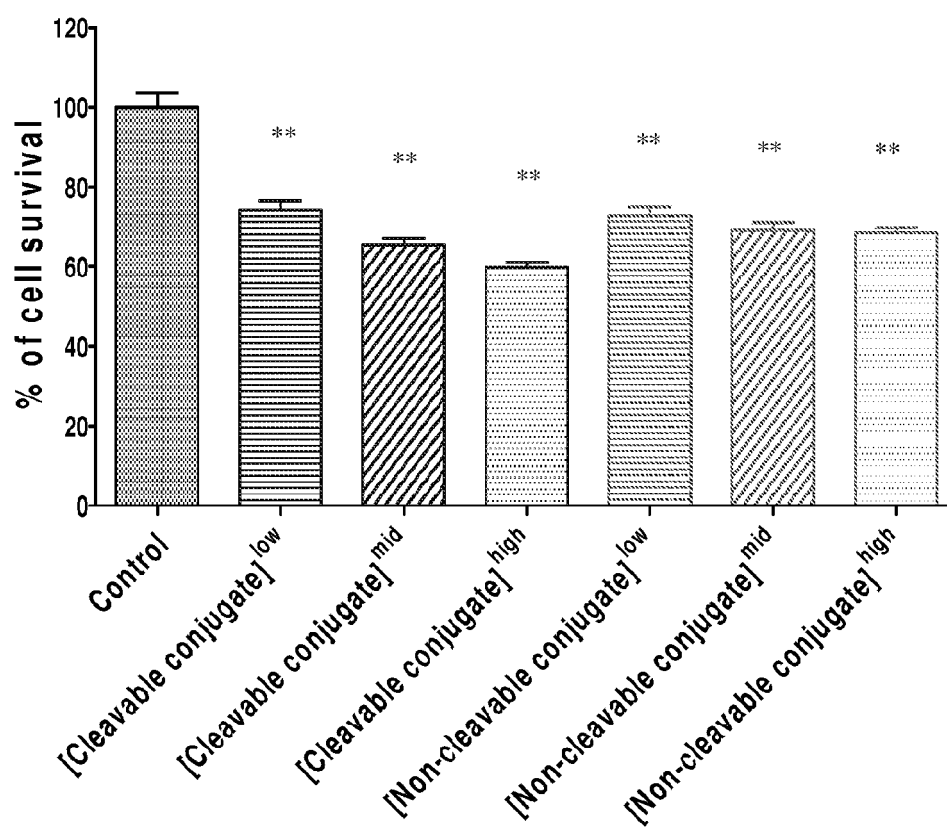
*, $p < 0.05$ compare to control; **, $p < 0.001$ compare to control

Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 17

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MTT Assay – Breast Cancer cell line MCF-7

** , $p < 0.001$ compare to control

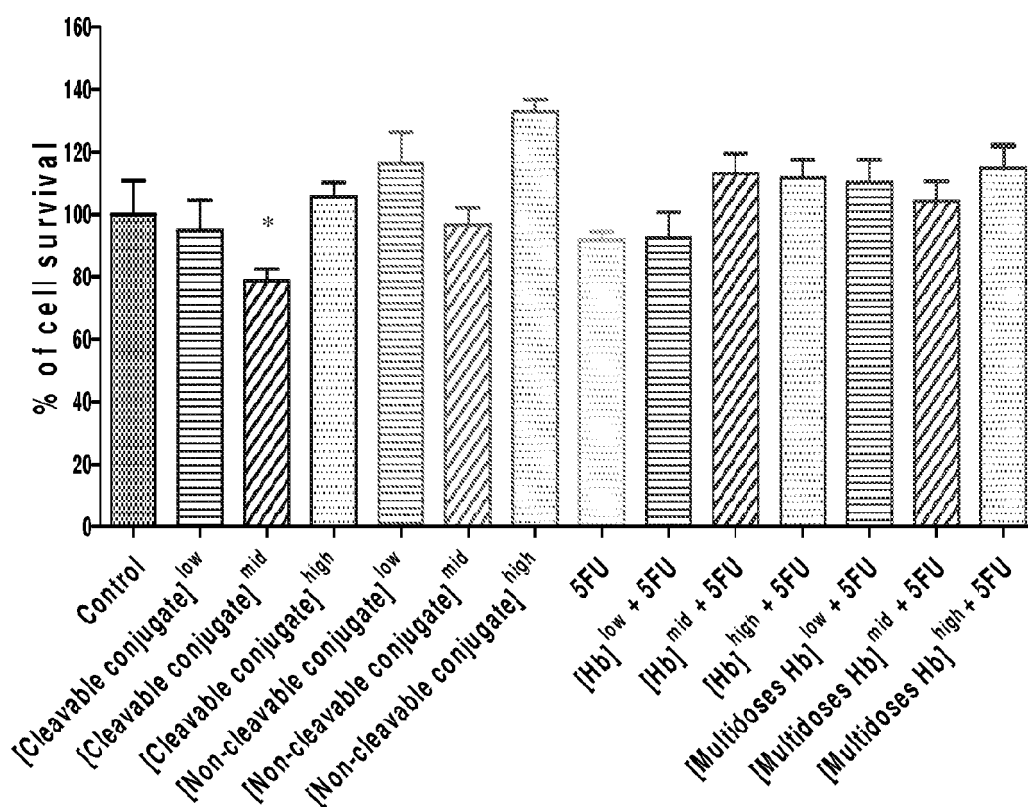
Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 18

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MTT Assay – Liver Cancer cell line Huh-7



*, $p < 0.05$ compare to control

Cleavable conjugate: Hb-5FU-carbinolamine (cleavable) conjugate;

Non-cleavable conjugate: Hb-5FU-alkyl (non-cleavable) conjugate.

FIG. 19

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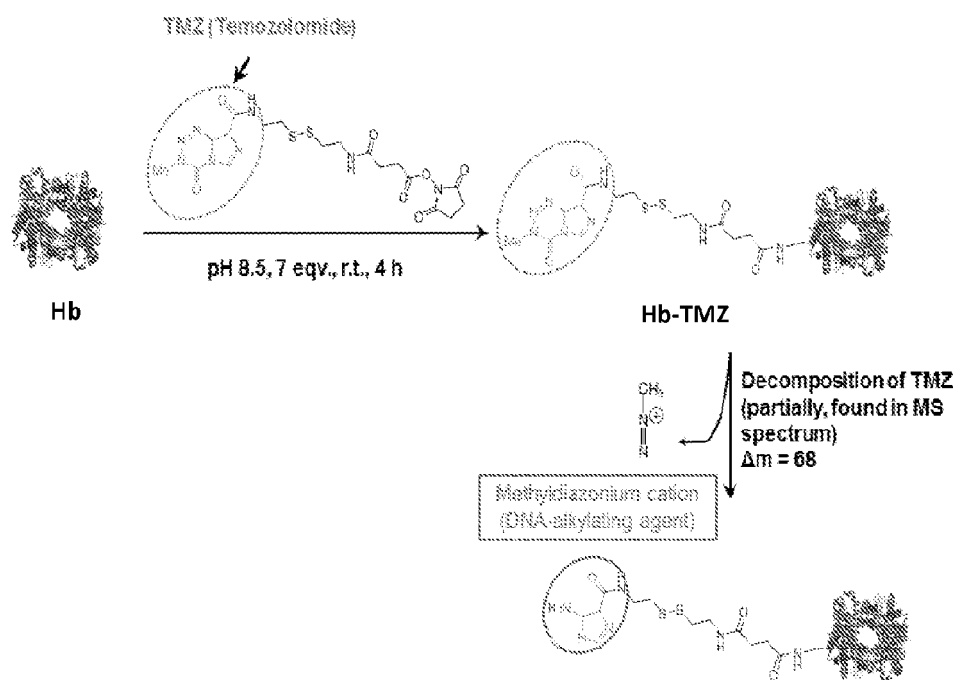


FIG. 20

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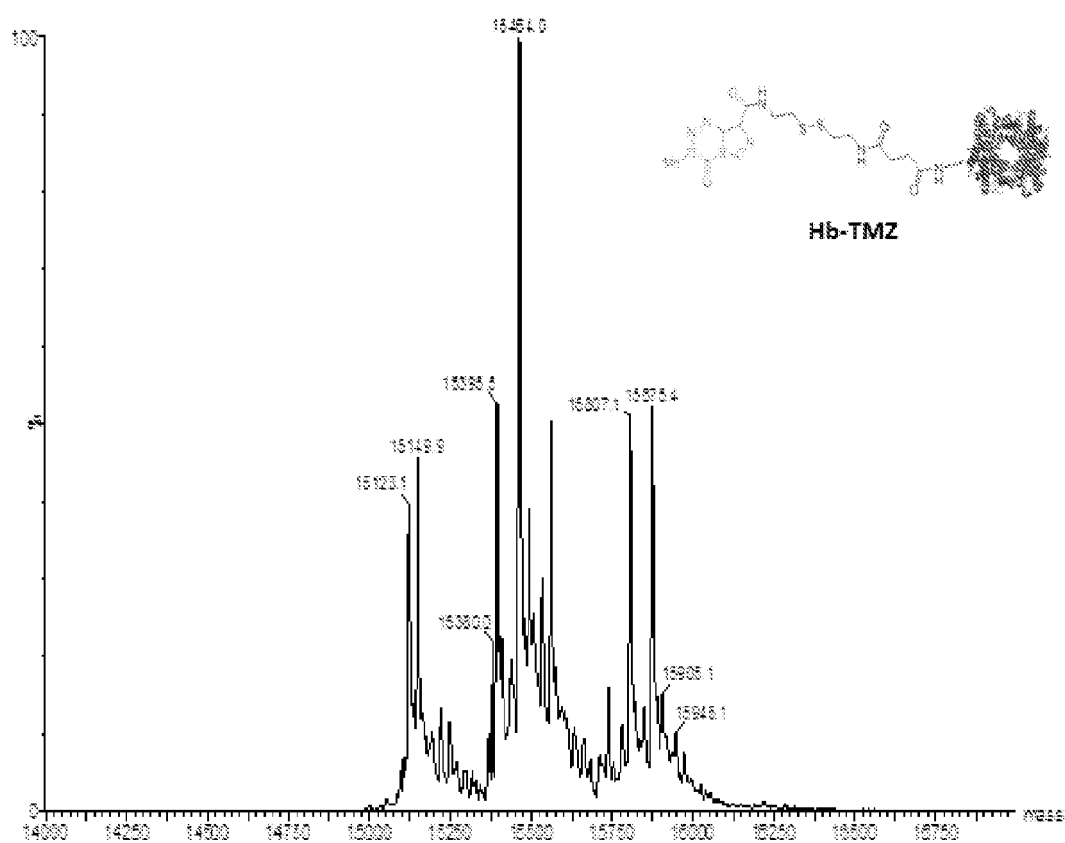


FIG. 21

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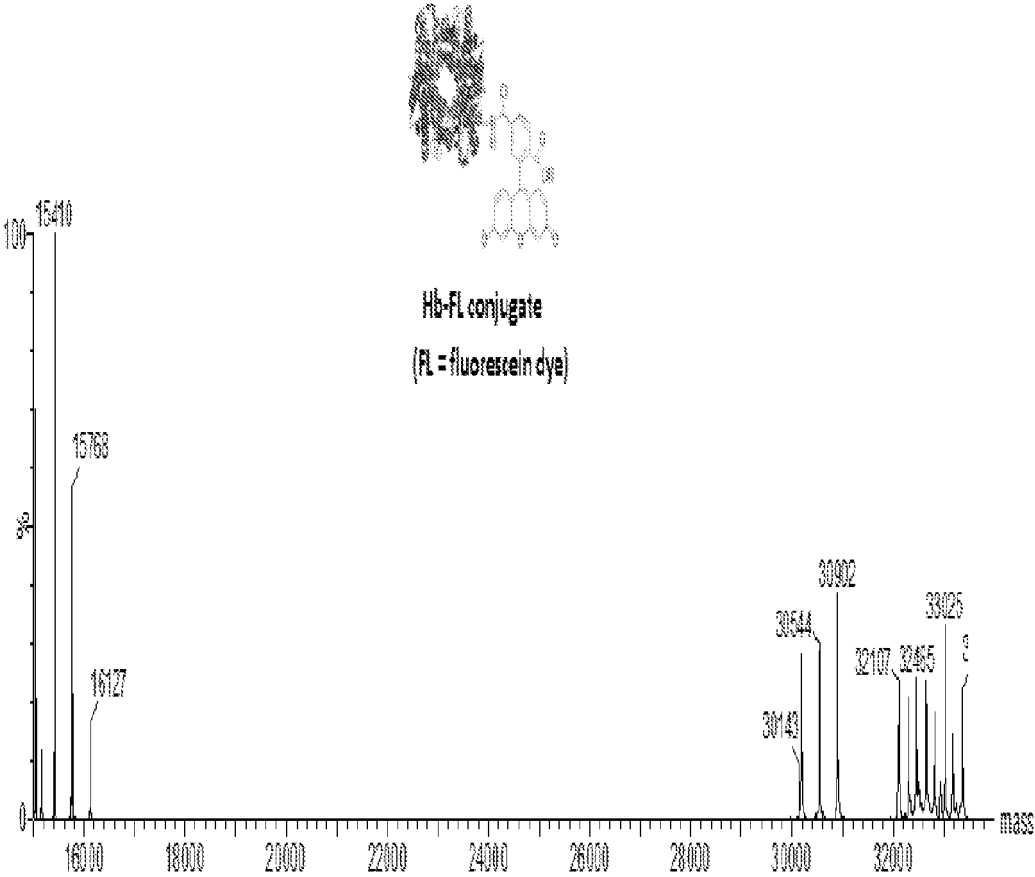


FIG. 22

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(A)

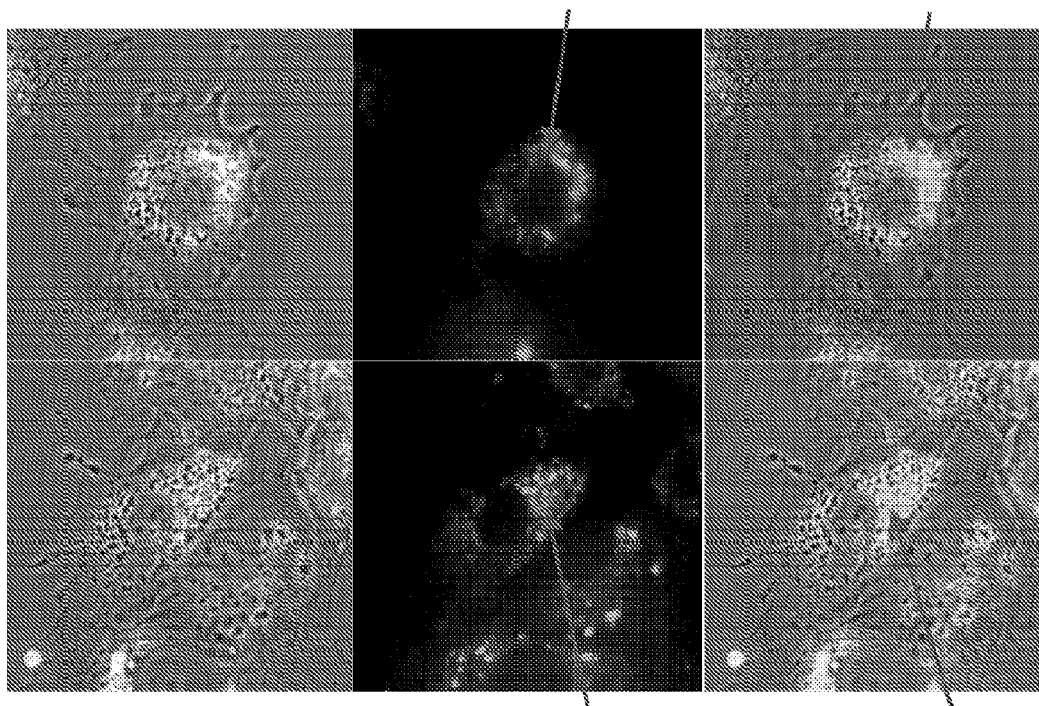
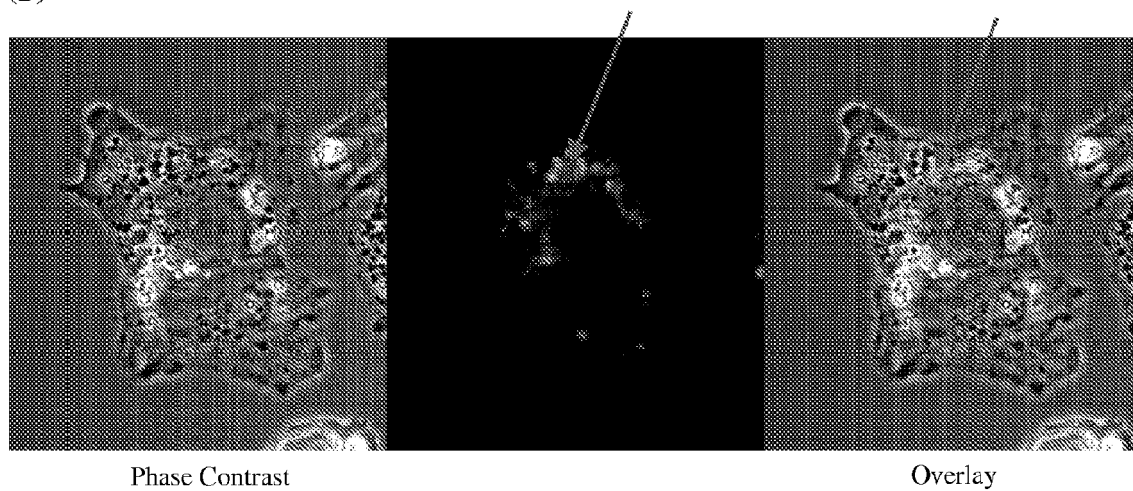


FIG. 23

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(B)



Phase Contrast

Overlay

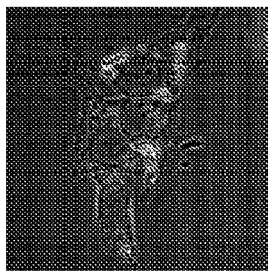
**Hb-5FU-alkyl(non-cleavable)-FL
conjugate, labeled with
one fluorescent dye**

FIG. 23 (cont'd)

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Hb-5Fu-Dan-TAM conjugate, labeled with two fluorescent dyes

(C)



Phase contrast



Excitation for
TAM dye

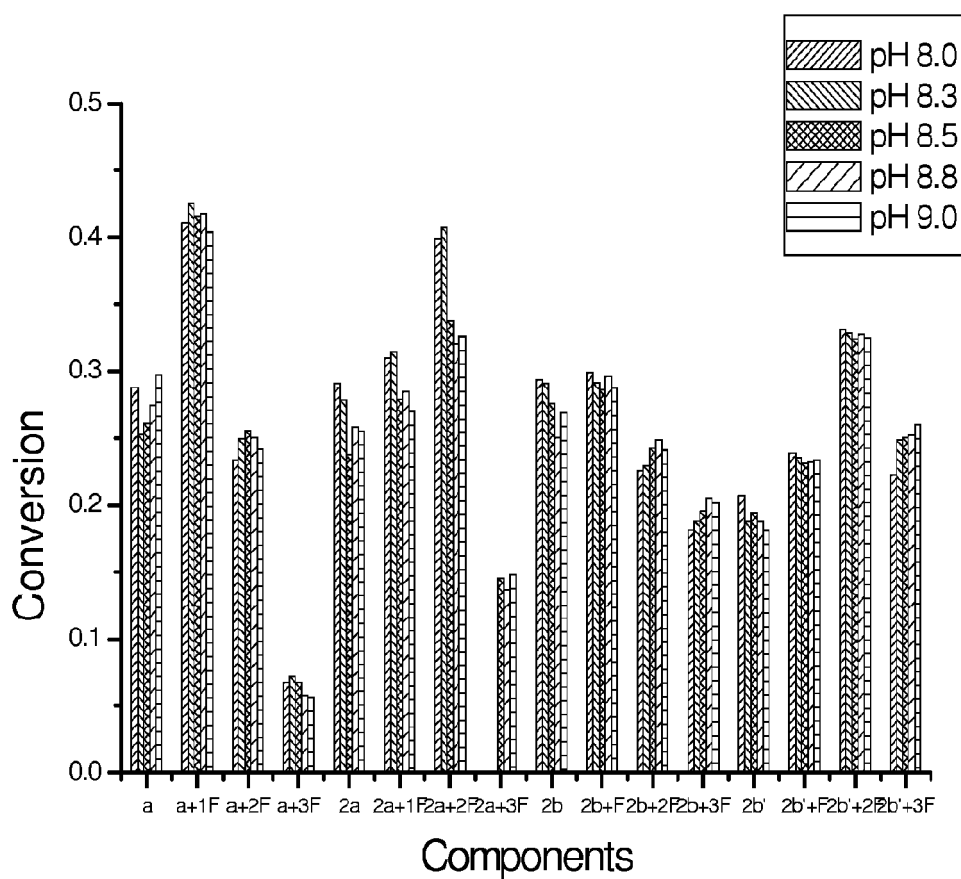
Excitation
for Dan dye



Overlay for TAM
dye and Dan dye

FIG. 23 (cont'd)

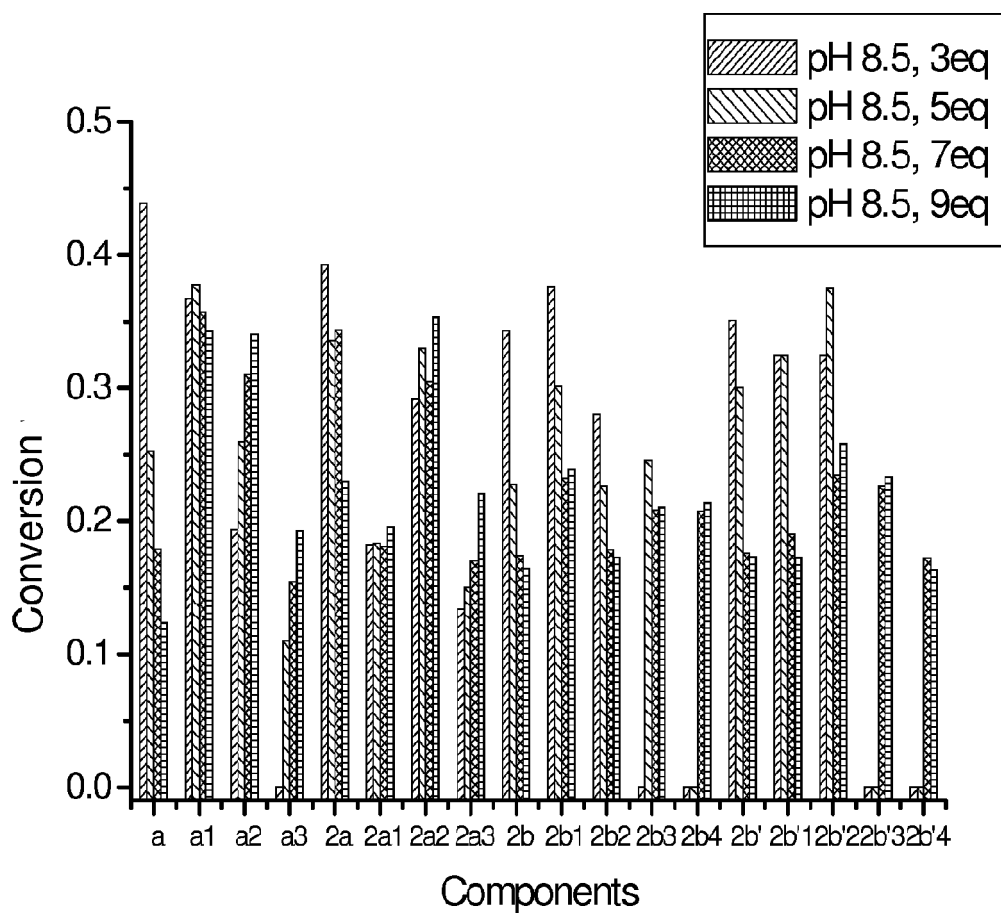
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a = α chain, a1 = α chain modified with mono-fluorescein, a2 = α chain modified with di-fluorescein, a3 = α chain modified with tri-fluorescein, 2a = α - α chain, 2a1 = α - α chain modified with mono-fluorescein, 2a2 = α - α chain modified with di-fluorescein, 2a3 = α - α chain modified with tri-fluorescein, 2 β = β - β chain, 2 β 1 = β - β chain modified with mono-fluorescein, 2 β 2 = β - β chain modified with di-fluorescein, 2 β 3 = β - β chain modified with tri-fluorescein, 2 β 4 = β - β chain modified with tetra-fluorescein, 2 β' = β' - β' chain, 2 β' 1 = β' - β' chain modified with mono-fluorescein, 2 β' 2 = β' - β' chain modified with di-fluorescein, 2 β' 3 = β' - β' chain modified with tri-fluorescein, 2 β' 4 = β' - β' chain modified with tetra-fluorescein.

FIG. 24

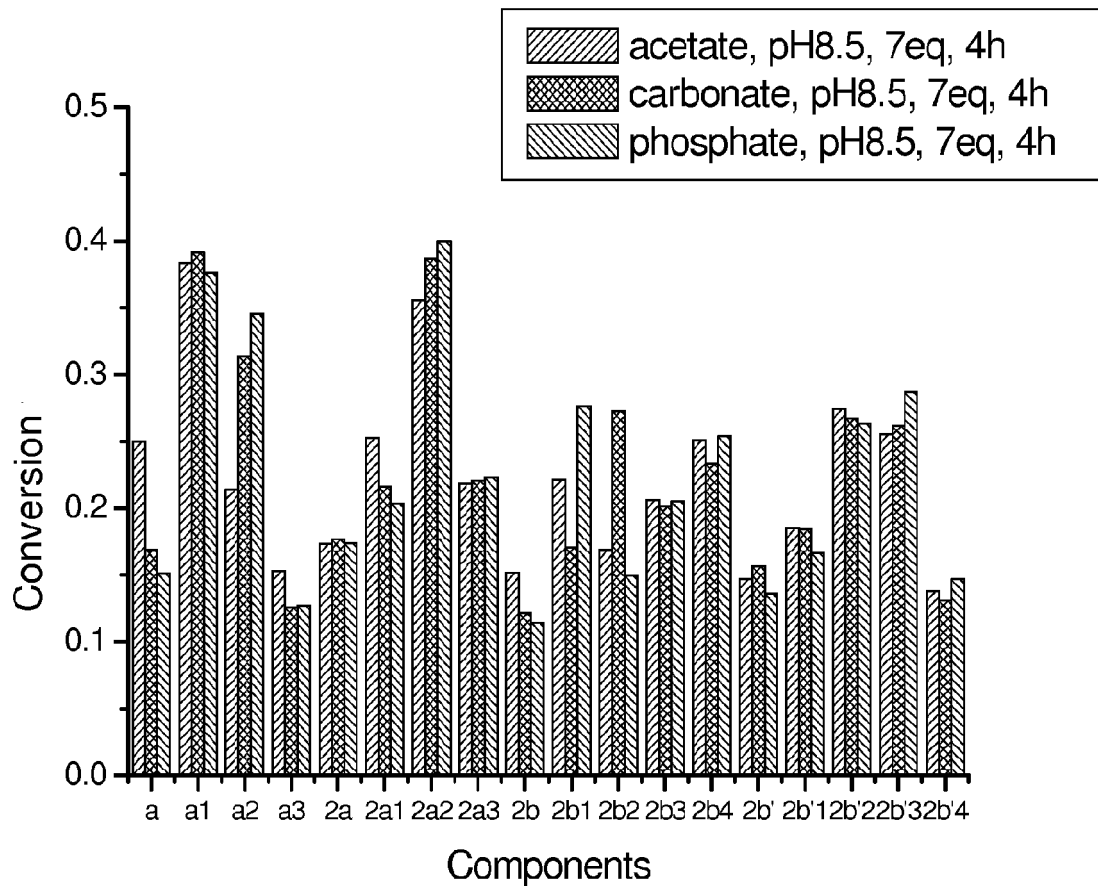
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a = α chain, a1 = α chain modified with mono-fluorescein, a2 = α chain modified with di-fluorescein, a3 = α chain modified with tri-fluorescein, 2a = α - α chain, 2a1 = α - α chain modified with mono-fluorescein, 2a2 = α - α chain modified with di-fluorescein, 2a3 = α - α chain modified with tri-fluorescein, 2 β = β - β chain, 2 β 1 = β - β chain modified with mono-fluorescein, 2 β 2 = β - β chain modified with di-fluorescein, 2 β 3 = β - β chain modified with tri-fluorescein, 2 β 4 = β - β chain modified with tetra-fluorescein, 2 β' = β' - β' chain, 2 β' 1 = β' - β' chain modified with mono-fluorescein, 2 β' 2 = β' - β' chain modified with di-fluorescein, 2 β' 3 = β' - β' chain modified with tri-fluorescein, 2 β' 4 = β' - β' chain modified with tetra-fluorescein.

FIG. 25

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a = α chain, a1 = α chain modified with mono-fluorescein, a2 = α chain modified with di-fluorescein, a3 = α chain modified with tri-fluorescein, 2a = α - α chain, 2a1 = α - α chain modified with mono-fluorescein, 2a2 = α - α chain modified with di-fluorescein, 2a3 = α - α chain modified with tri-fluorescein, 2 β = β - β chain, 2 β 1 = β - β chain modified with mono-fluorescein, 2 β 2 = β - β chain modified with di-fluorescein, 2 β 3 = β - β chain modified with tri-fluorescein, 2 β 4 = β - β chain modified with tetra-fluorescein, 2 β' = β' - β' chain, 2 β' 1 = β' - β' chain modified with mono-fluorescein, 2 β' 2 = β' - β' chain modified with di-fluorescein, 2 β' 3 = β' - β' chain modified with tri-fluorescein, 2 β' 4 = β' - β' chain modified with tetra-fluorescein.

FIG. 26

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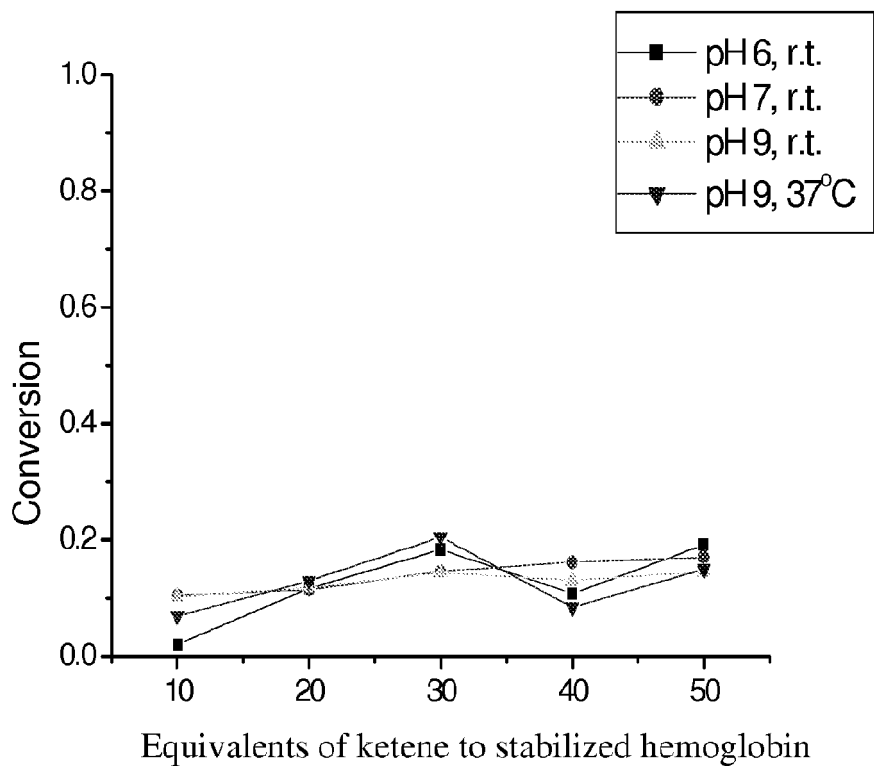
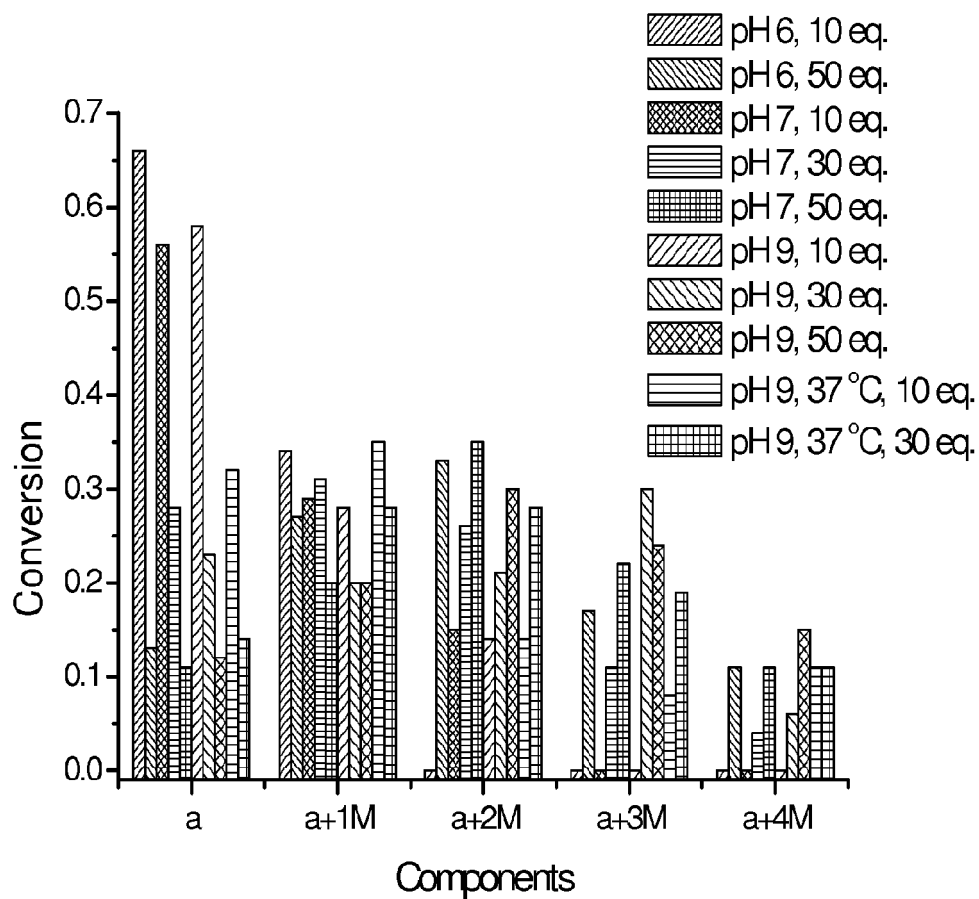


FIG. 27

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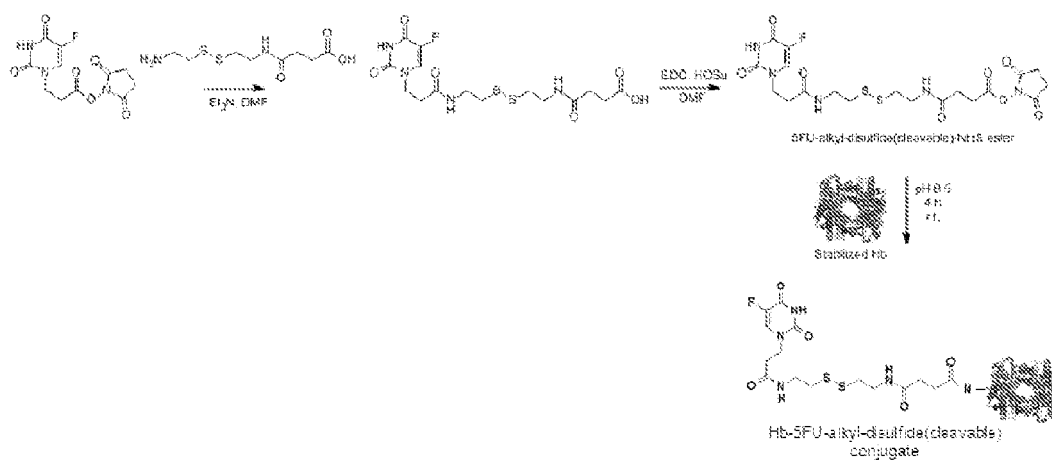
a = α chain,
 a+1M = α chain modified with mono-anhydride
 a+2M = α chain modified with di-anhydride
 a+3M = α chain modified with tri-anhydride
 a+4M = α chain modified with tetra-anhydride

FIG. 28

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Disulfide

(A)



(B)

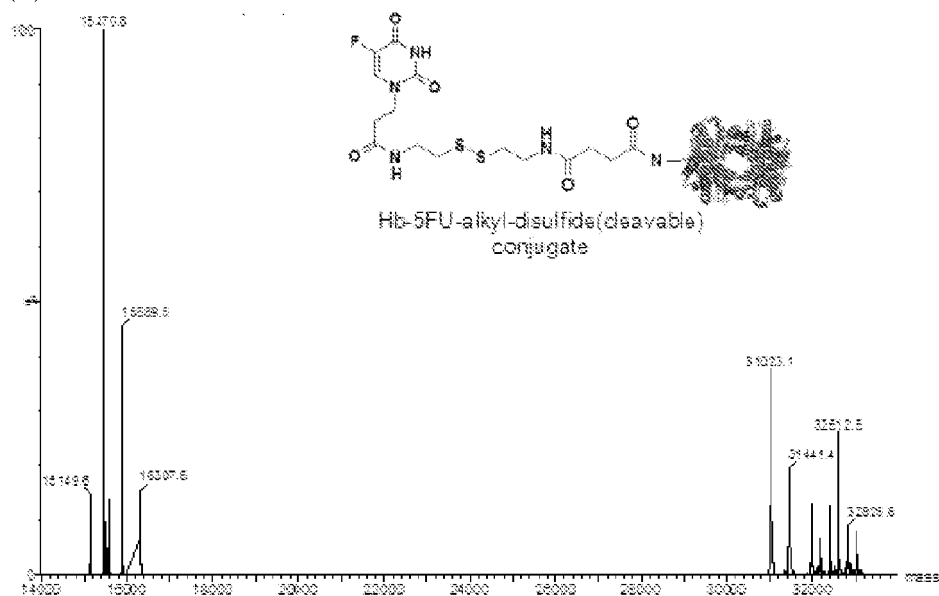


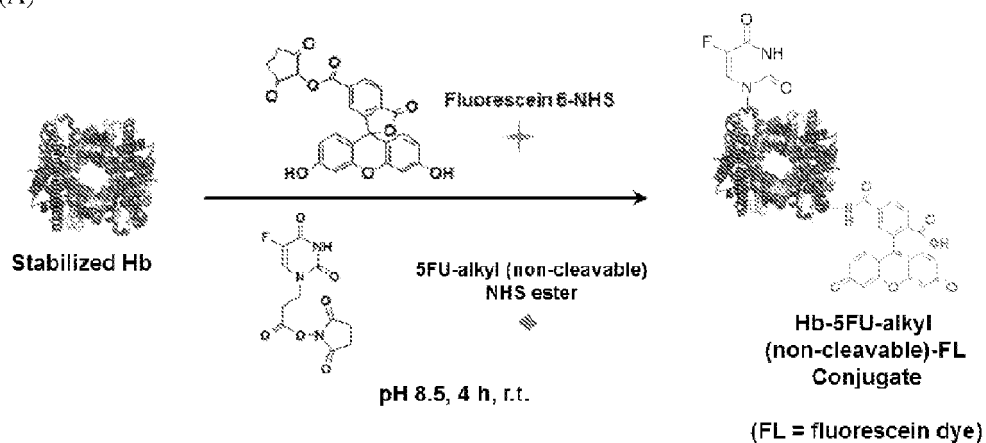
FIG. 29

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One-Dye compound – Hemoglobin labeled with 5FU (non-cleavable) and Fluorescein
 Name = Hb-5FU-alkyl (non-cleavable)-FL conjugate

Modification:

(A)



(B)

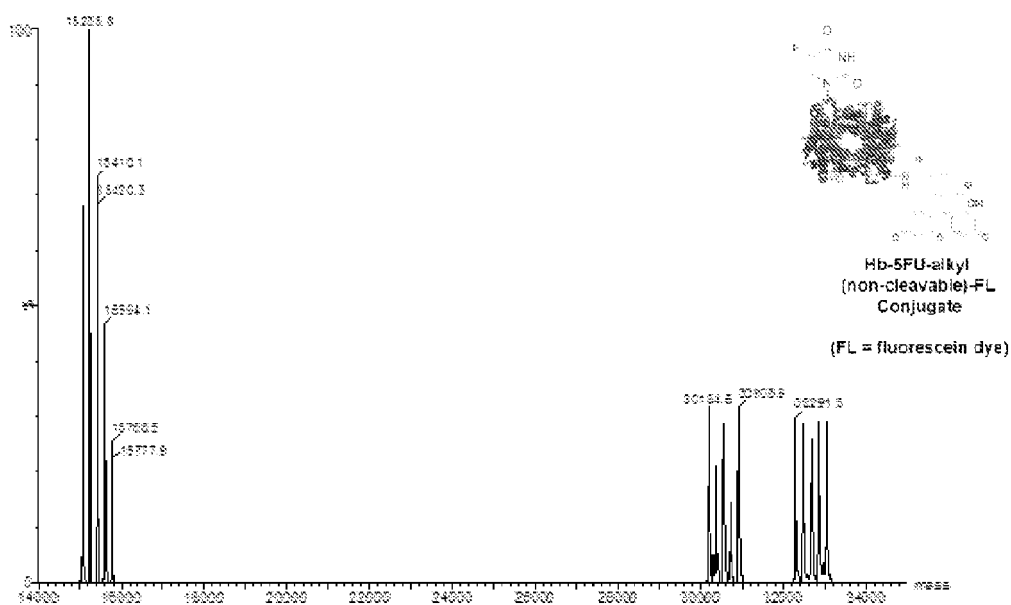


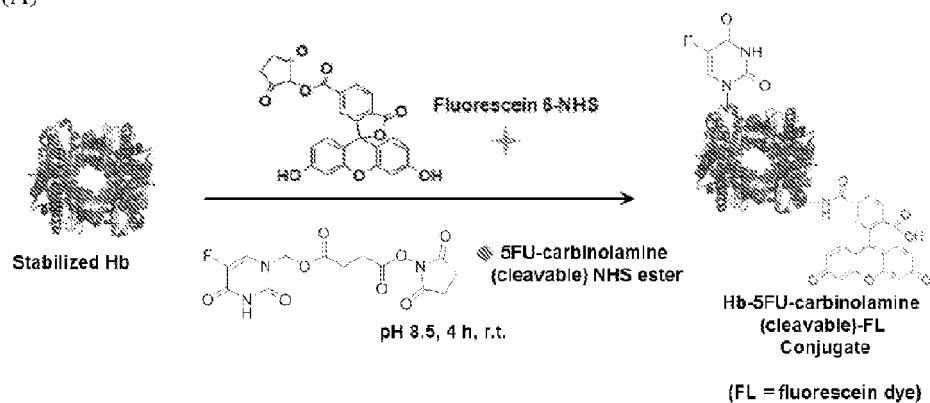
FIG. 30

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One-Dye conjugate for imaging – Hemoglobin labeled with 5FU (cleavable) and Fluorescein
 Name = Hb-5FU-carbinolamine (cleavable)-FL conjugate

Modification:

(A)



(B)

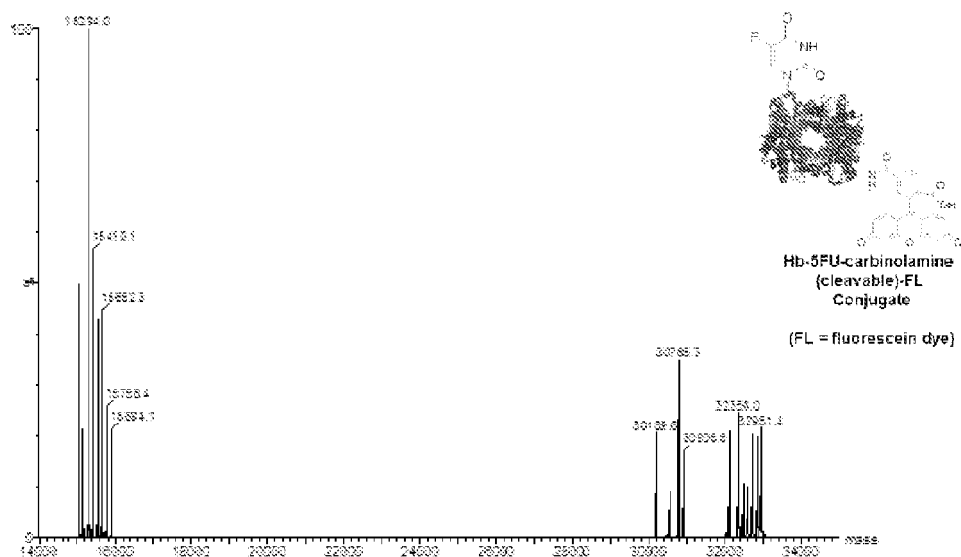
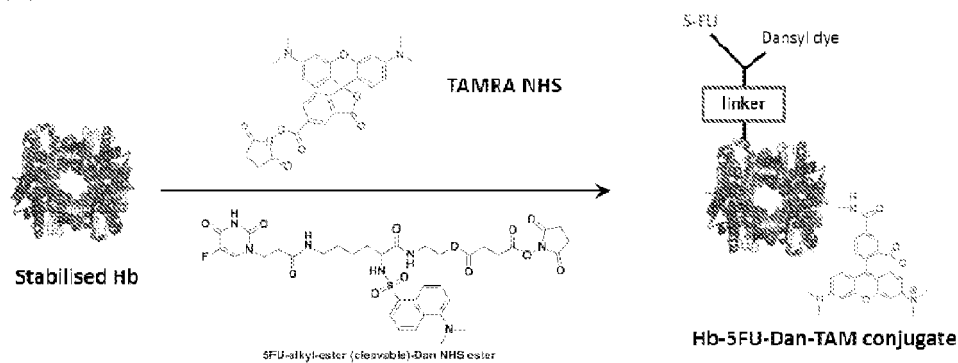


FIG. 31

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Two-dyes conjugate for imaging
Name: Hb-5FU-Dan-TAM conjugate

(A)



(B)

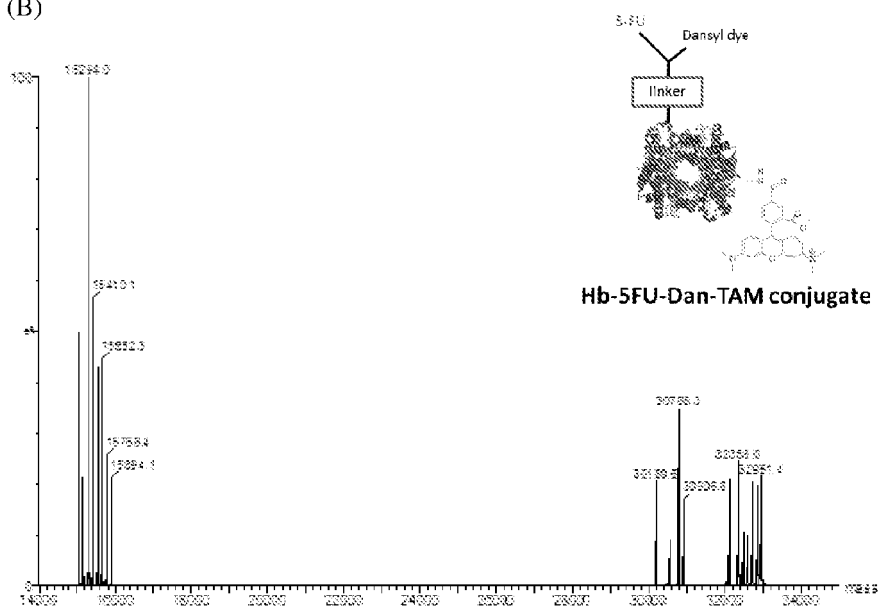


FIG. 32