NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

IR CHARACTERISATION

S.NO.	CHARACTERIZATION OF	v (cm-1)	Remarks
1.1	Drug (Docetaxel)	1710.16	saturated carboxylic acids, C=O
1.2		1245	C-O
1.3		706.99	C-H Aromatic
2	**Polymer (PEG 43000)**	1101.90	C-O-C
3	**Interferon alpha 2a**	1652.90	NH2
4.1	**VRP007 (Formulation 7)**	1716.18	C=O
4.2		1090	C-O-C
4.3		1652.82	NH2

FIG. 1

NMR CHARACTERISATION

S. No.	NMR characterization of	δ(ppm)	Remarks
1.1	Drug (Docetaxel)	4.43 (single peak)	Characteristics peaks of Docetaxel
1.2		5.59	
1.3		7.32	
1.4		2.0	
2	Polymer (PEG 43000)	3.75	PEG (single peak)
3	Drug +Polymer :	3.77ppm	Peak shift due to Docetaxel NH group bind with PEG
4	VRP007 **(Formulation 7)**	4.49	VRP 007 drug bind with NH C=0 and OH active site

FIG. 2

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

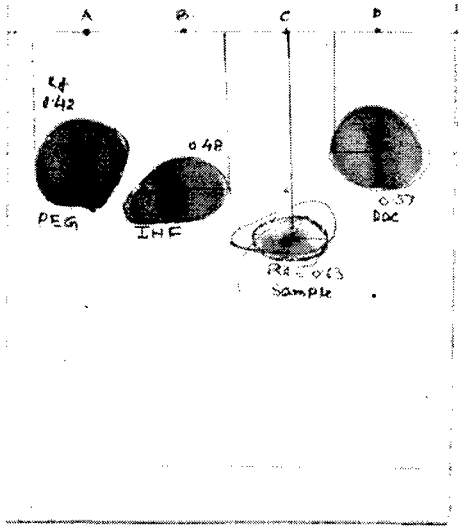


FIG. 3

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

REAL TIME STABILITY DATA

Name of Product:	F-6		
Strength:	Each ml contains Docetaxel Anhydrous equivalent to Docetaxel .....20 mg Interferon α-2a.....0.45 MIU	**Date of Mfg:**	APR-2011
Batch No :	VRP 6/11E01	**Date of Exp:**	APR-2013
Storage:	2-8°C	**Specification:**	In house

Period (months)	**Description (Clear colorless viscous liquid)**	**Identification**	**Assay**	
		BY HPLC	**Docetaxel (90% -110%)**	**Interferon α-2a (90% -110%)**
Initial	Complies	Complies	101.7%	100.6%
3	Complies	Complies	101.5%	99.94%
6	Complies	Complies	100.2%	99.53%

FIG. 4

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

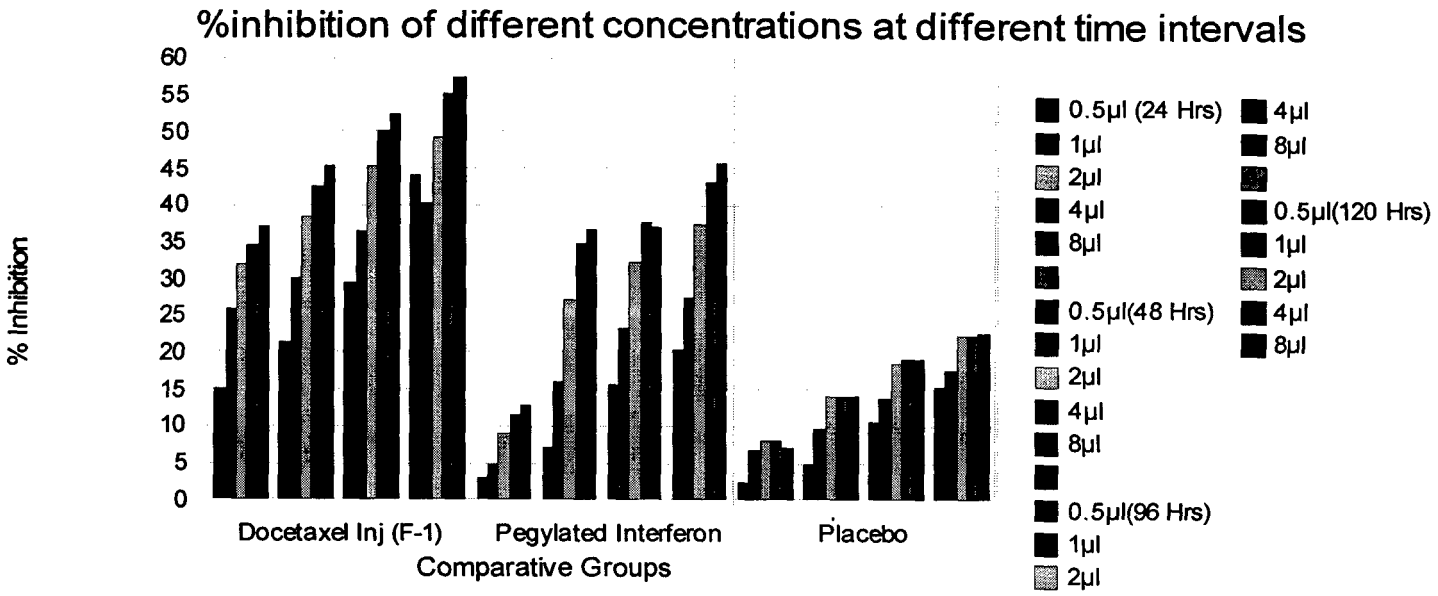


FIG. 5A

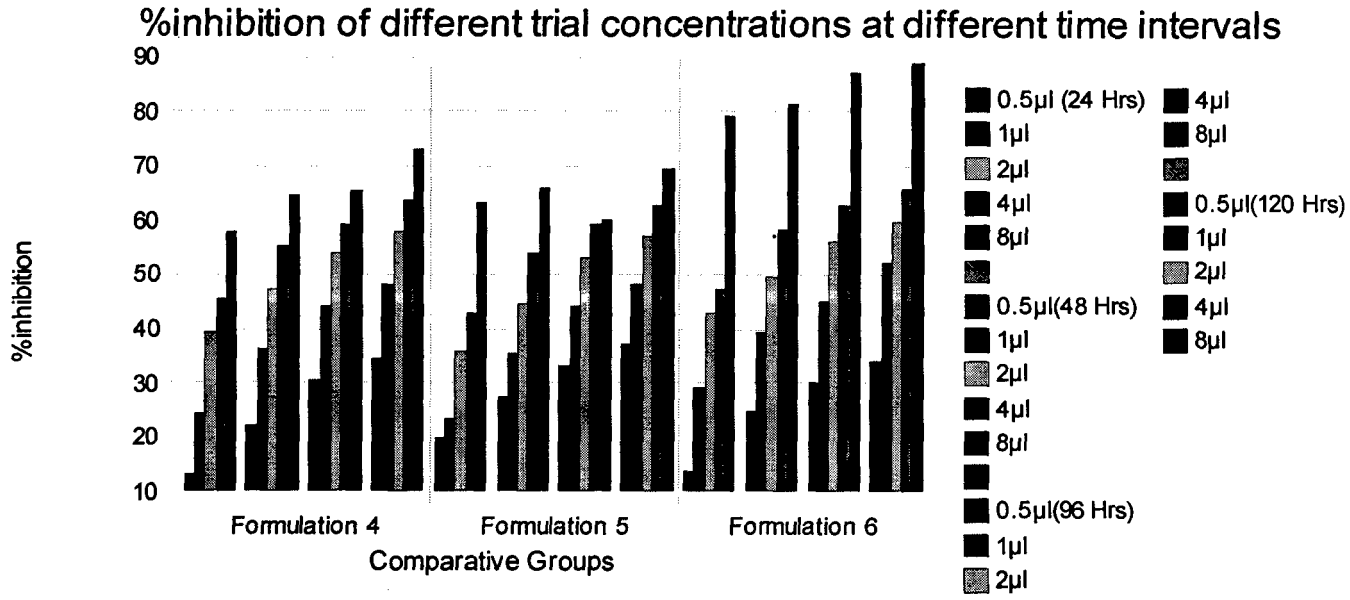


FIG. 5B

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

Code of sample	Volume of cell culture	Viable Cell count with proliferation after Incubation period 24Hrs at different concentration of drug					Viable Cell count with proliferation after Incubation period 48 Hrs at different concentration of drug					Viable Cell count with proliferation after Incubation period 96 Hrs at different concentration of drug					Viable Cell count with proliferation after Incubation period 120 Hrs at different concentration of drug				
		0.5	1	2	4	8	0.5	1	2	4	8	0.5	1	2	4	8	0.5	1	2	4	8
F-1	0.2 ml	4246	3703	3484	3274	3107	3921	3499	3087	2921	2722	3534	3180	2735	2493	2337	2794	2983	2540	2245	2100
F-2	0.2 ml	4885	4745	4544	4421	4327	4677	4195	3639	3265	2930	4252	3823	3378	3110	3009	4004	3623	3127	2836	2712
F-3	0.2 ml	4885	4766	4696	4691	4656	4755	4521	4498	4421	4402	4464	4312	4066	3936	3901	4229	4123	3877	3774	3632
F-4	0.2 ml	4334	3791	3029	2723	1624	3901	3177	2621	2231	1488	3473	2797	2291	2038	1290	3279	2583	2108	1822	1028
F-5	0.2 ml	3992	3835	3213	2863	1452	3625	3232	2755	2299	1321	3325	2786	2342	2039	1288	3124	2593	2150	1855	1097
F-6	0.2 ml	4307	3528	2854	2635	1032	3754	3021	2510	2088	980	3483	2736	2190	1847	876	3289	2382	2002	1697	675
7 (Cellline)	----	5000																			

FIG. 6

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

Code of sample	Volume of cell culture	Viability (%) after Incubation period 24Hrs at different concentration of drug					Viability (%) after Incubation period 48 Hrs at different concentration of drug					Viability (%) after Incubation period 96 Hrs at different concentration of drug					Viability (%) after Incubation period 120Hrs at different concentration of drug				
		0.5	1	2	4	8	0.5	1	2	4	8	0.5	1	2	4	8	0.5	1	2	4	8
F-1	0.2 ml	84.93	74.08	69.70	65.49	62.14	78.44	70.00	61.77	58.44	54.43	70.70	63.63	54.74	49.89	42.83	55.90	59.70	50.84	44.93	38.48
F-2	0.2 ml	97	95	91	88.44	86.54	92.88	84.00	72.88	65.33	58.57	84.44	76.56	67.67	62.23	63.09	79.53	72.57	62.65	56.75	51.14
F-3	0.2 ml	97.71	93.33	92	89.84	93.12	95.11	90.44	86.05	80.44	76.05	89.29	86.26	81.41	74.74	66.23	84.59	82.48	77.63	71.51	66.57
F-4	0.2 ml	86.7	75.83	60.59	54.46	32.48	78.04	63.55	52.44	44.66	29.75	69.49	55.95	45.85	40.80	35.37	65.61	51.68	42.19	36.49	29.07
F-5	0.2 ml	80.0	76.70	64.27	57.26	29.04	72.66	64.66	55.11	46.00	26.41	66.66	55.75	46.86	40.80	39.78	62.65	51.89	43.03	37.13	31.62
F-6	0.2 ml	86.16	70.57	57.1	52.7	20.64	75.11	60.44	50.22	41.77	19.59	69.69	54.74	43.83	36.96	13.03	65.82	47.67	40.08	33.96	11.16

FIG. 7

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

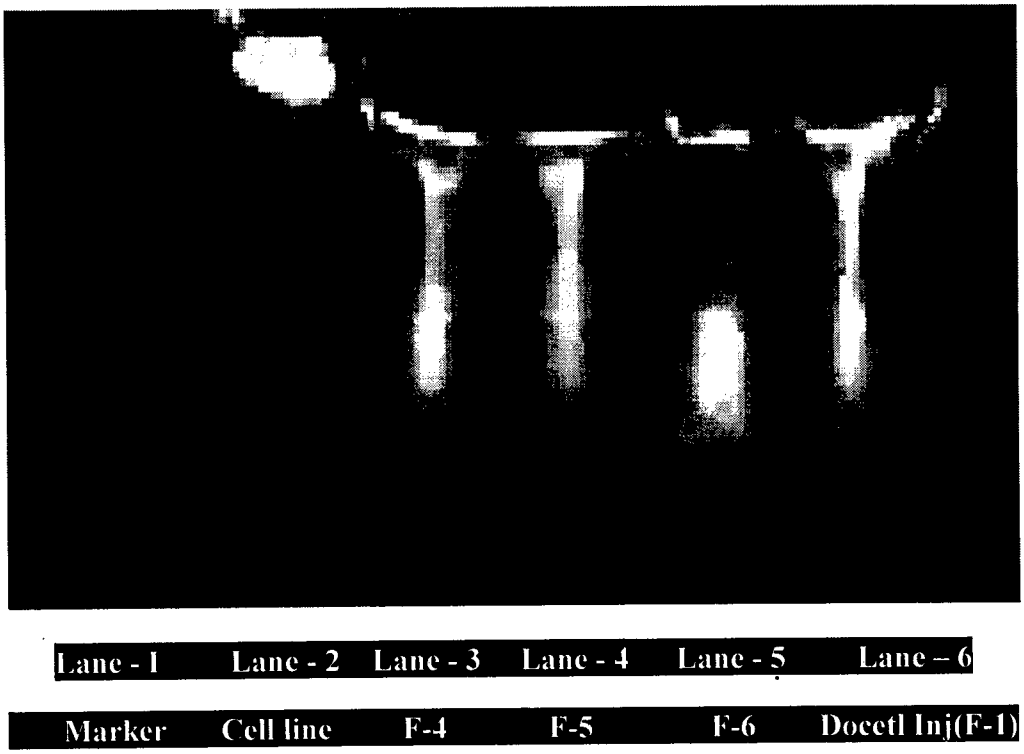


FIG. 8

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

Time	Docetaxel In Vitro Release (µg/ ml) F1-Docetaxel injection,F-5 Formulation 5, F6- Formulation 6, F 4- Formulation 4			
Time	F1	F5	F6	F4
10 Min.	2.34	0.75	1.53	1.35
20 Min.	2.02	0.65	1.58	1.33
1 Hr.	2.18	1.7	2.83	1.81
2 Hr.	2.06	1.64	2.96	1.64
4 Hr.	1.84	0.89	2.61	1.28
6 Hr.	1.62	0.74	2.37	1.08
8 Hr.	1.03	0.68	1.96	1.05

FIG. 9

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

Comparative percentage of tumor growth in DMBA induced breast cancer model				
	0 days	**4th days**	**8th days**	**12th days**
Healthy Control group (n=8)	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Breast cancer induced untreated group (n=8)	100.0 ± 45.12	187.26 ± 22.81***	250.14± 20.0***	282.55± 22.19***
Docetaxel group (n=8)	100.0 ± 21.58	149.41 ±15.41***	122.27 ± 12.74*	98.68 ± 12.35ns
Docetaxel + pegylated Inf α 2a (n 8)	100.0 ± 27.89	138.41 ± 22.10**	104.09± 12.45ns	87.03 ± 10.63ns
F-6 group (n=8)	100.0 ±22.15	81.21 ± 11.74*	64.64 ± 11.40**	45.36 ± 7.96***

FIG. 10

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

Comparative Effect of Different Comparative groups on tumor volume (cm) Reduction in Breast cancer Model				
	0 days	4th days	8th days	12th days
Control group (n=8)	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Breast cancer induced (n=8)	2.48 ± 1.10	4.36 ± 1.01*	6.41± 1.21***	7.56± 1.72***
Docetaxel group (n=8)	2.36 ± 0.57	2.07.± 0.45ns	1.62 ± 0.40*	1.49 ± 0.37*
Docetaxel + pegylated Inf α 2a group (n =8)	2.68 ±0 .74	2.18± 0.37ns	1.79 ± 0.48*	1.24 ±0 .70**
F-6 group (n=8)	2.98 ±0.61	2.28 ± 0.44***	0.98 ± 0.38***	0.61 ± 0.18***

FIG. 11

NOVEL CONJUGATES FOR TARGETED DRUG DELIVERY

Comparative Adverse effect of Docetaxel, Docetaxel + pegylated interferon and F-6 on Breast cancer rat model after 12 days								
Symptoms	Alopecia	Neutropenia	Fluid Retention	Diarrohea	Vomiting	Anemia	Neurosensory	Score card after 12 days treatment of drugs in breast cancer 5 (severe), 4 (moderate), 3 (mild), 2 (minimal) ; 1 (nil) .
Control group (n=8)	Nil	Nil	Nil	Nil	Nil	Nil	Nil	
Breast cancer induced (n=8)	Nil	Nil	Nil	Nil	1	1	Nil	
Docetaxel group (n=8)	5	5	4	5	4	4	3	
Docetaxel + pegylated INF (n =8)	3	4	4	3	3	3	3	
F-6 group (n=8)	2	2	1	1	1	2	1	

FIG. 12

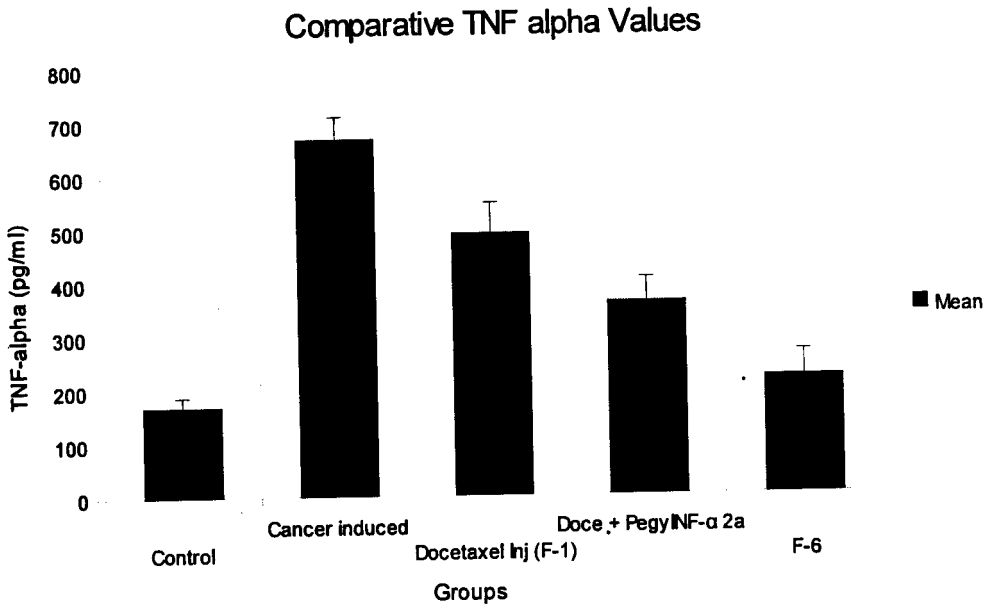

Comparative TNF alpha Values
800
700
600
500
400
300
200
100
0
TNF-alpha (pg/ml)
Mean
Control
Cancer induced
Docetaxel Inj (F-1)
Doce + PegyINF-α 2a
F-6
Groups

FIG 13