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LIGHT ASSISTED TIO2-BASED NANOCOMPOSITE SYSTEMS: A NOVEL TREATMENT FOR CANCER

Bharat Kwatra[1], Maanvi Mudgil[2]
State University of New York[1], Delhi University[2]

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Corresponding author: Bharat Kwatra
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Introduction

Cancer remains as one of the most dreaded diseases with millions of deaths each year worldwide. There has been a continuous wave of advances in cancer treatment. This study brings out a novel approach for cancer treatment using light explained by Photodynamic therapy (PDT) which is described as inserting an inactive form of a medicament or carrier system in a target issue which is activated on illumination with light. The resulting photochemical and photobiological processes cause irreversible damage of tumour tissues with minimized loss of healthy tissues. The use of TiO2-based nanoparticles (NPs) in a combination with Ru-complex as photo-tunable nanocomposite system (NCS) against A375 human melanoma cell line has been shown in previous studies. The Ru-complex releasing kinetics enhanced by illumination with UV light and sustained in presence of visible light was in correlation with cell cytotoxicity. It is known from other studies that the cellular uptake of nanoparticles depends on their size and shape. Therefore, the aim of this study was to test the differences in the UV-induced cytotoxicity of TiO2 nanoparticles of various size and shapes and on three different types of cancer cell lines.

Material and Methods

Metallo-drug complex cis-dichlorobis (2,2'-bipyridyl-4,4'-dicarboxylic acid) ruthenium(II) was synthesized, and was described by FT-IR, UV/VIS spectroscopy and with MALDI TOF mass spectrometry [2]. TiO_2 nanotubes (NT) and prolate nanospheroids (PNS) along with colloidal nanoparticles were synthesized using the modified hydrothermal procedure and were described by TEM. The nanocomposite system was prepared followed by separating nanoparticles loaded with complex from free standing molecules by centrifugation, Further, the bonded supernatant was determined by HPLC Chromatography. In vitro complex release test of nanocomposite system was performed. The following human cell cultures obtained from the ATCC were used: A375-melanoma, PANC1-pancreatic cancer and SKBR3-breast cancer. MDA assay in treated cell lines was used to estimate oxidative stress. Sulforodamine B assay was used to determine Cytotoxicity of cells, after incubation with nanoparticles and nanocomposite system, in the dark, and under UV light illumination.

Observation

Figure 1: shows the graph obtained by FT-IR

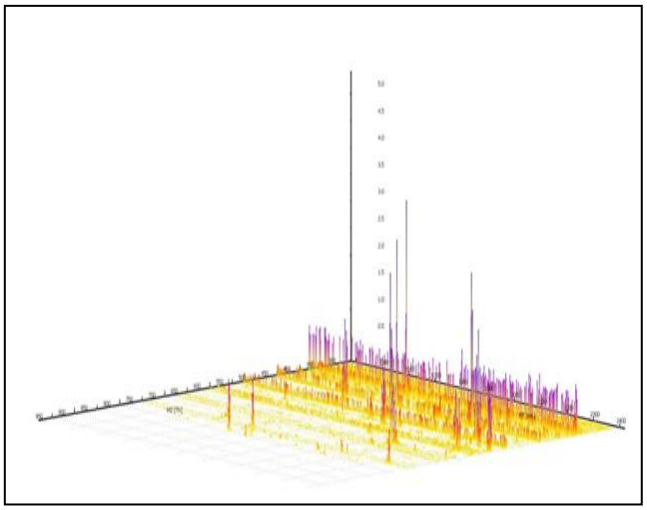

Figure 2: shows the graph obtained by MALDI TOF mass spectroscopy. These graphs helped in characterising the synthesis of the metallo-drug complex.

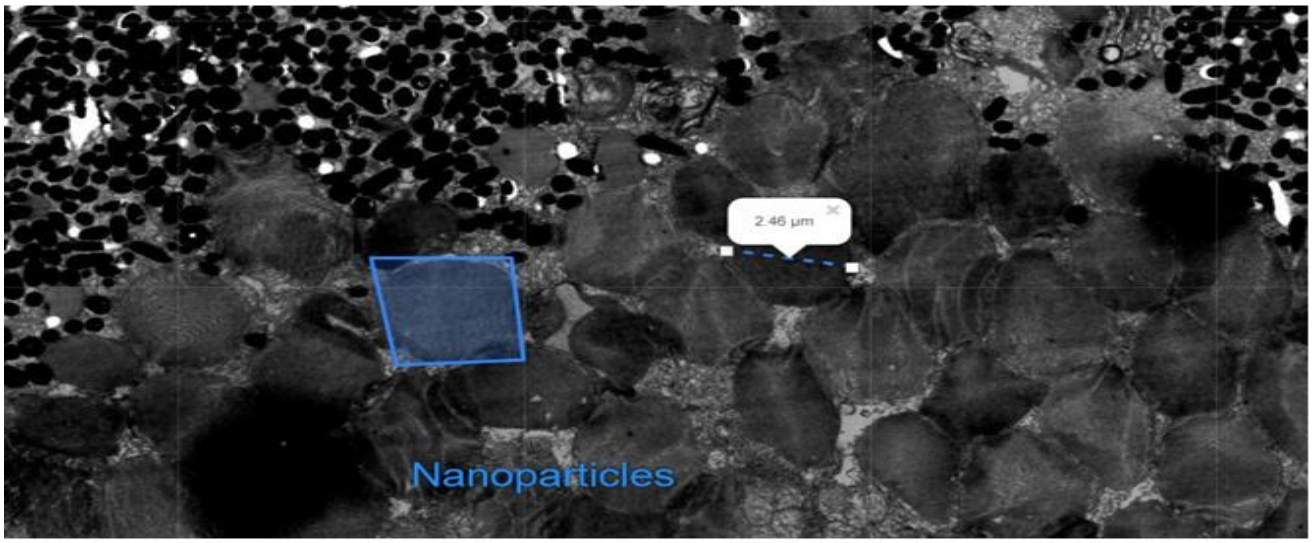

Figure 3: shows the observation from TEM which was used to characterize the synthesis of NT and PNS. TEM of nanoparticles showed the structure of wanted nanoparticles and determined size and shape of synthetized particles.

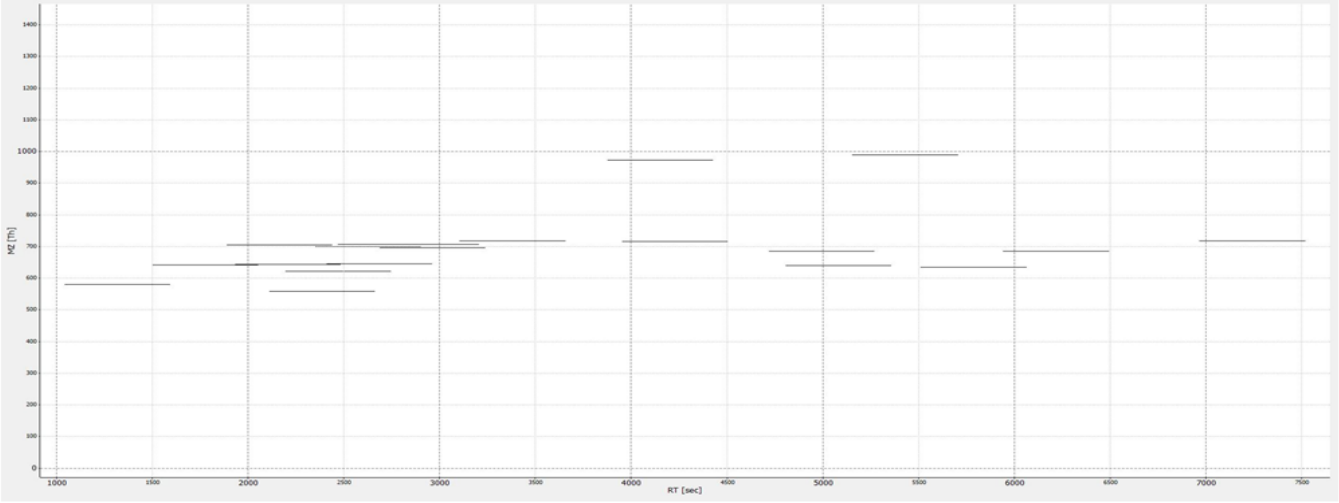

Figure 4: The chromatogram obtained by HPLC Chromatography for determination of bonded supernatant during preparation of NCS

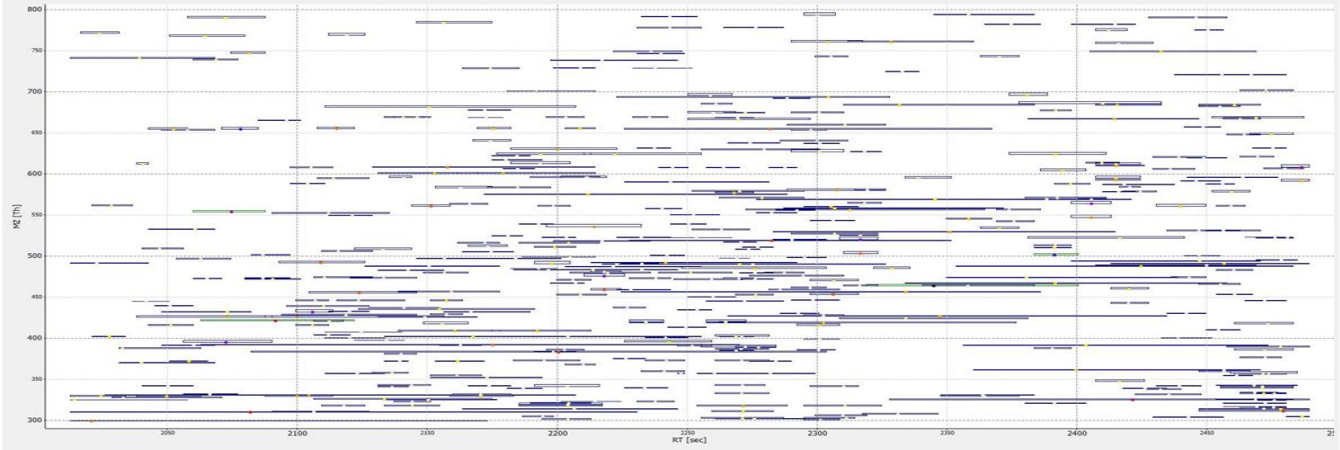

Figure 5: shows the graph of maxima spectra and

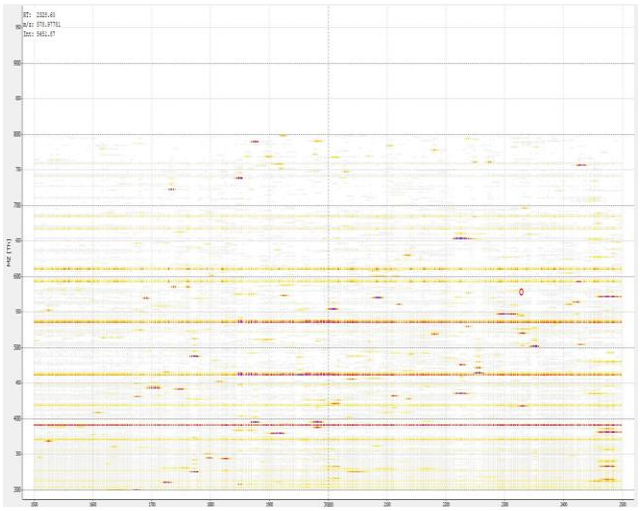

Figure 6: shows the spectra for metallo-drug

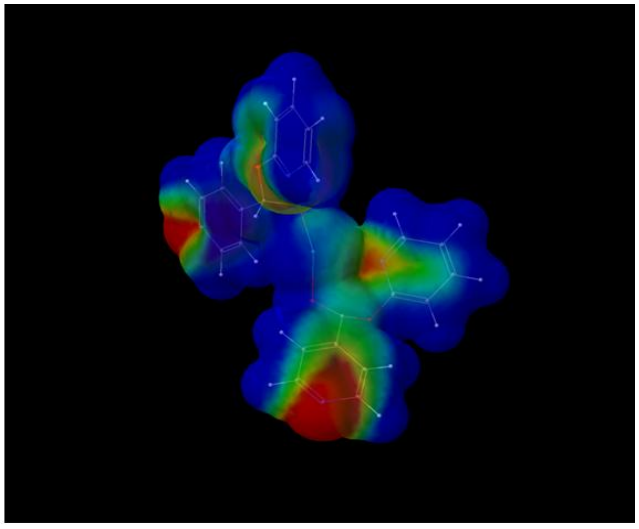

Figure 7: The molecular structure of metallo-drug complex is given in Figure 7.

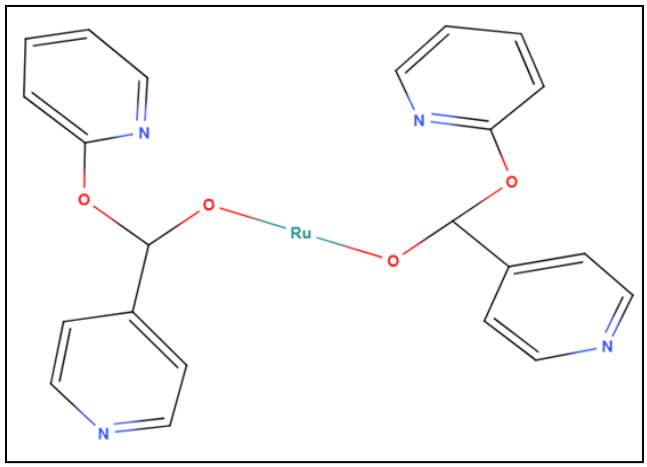

Figure 8: shows the nano-composite system of prolate nano-spheroids holding the metallo-drug and

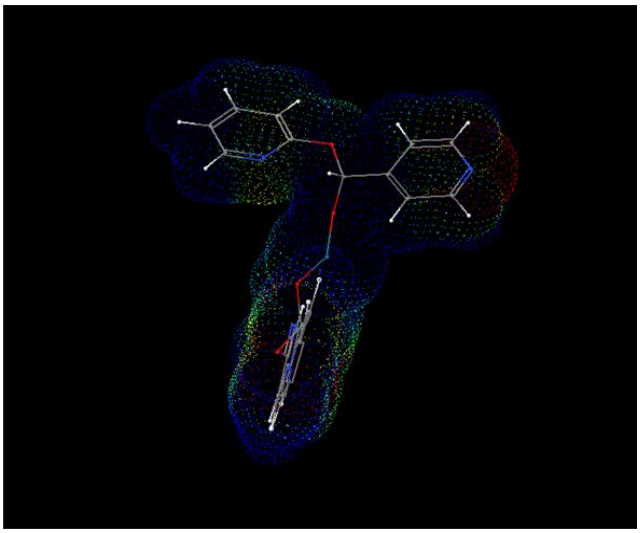

Figure 9: shows the shelled structure of the nano-composite system.

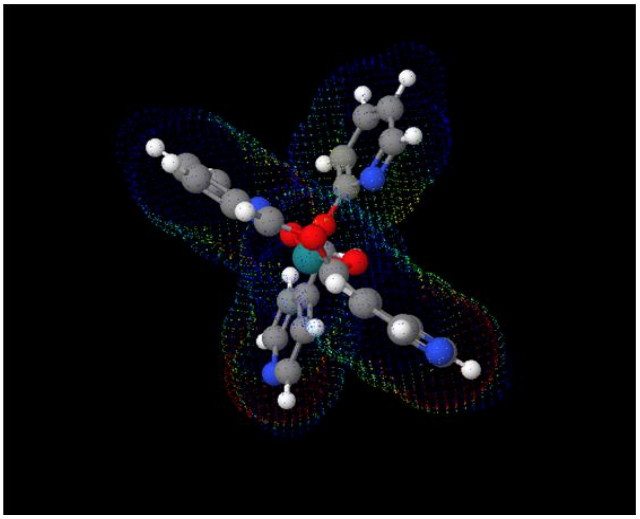

Figure 10: shows the nano-composite system nanotubes holding the metallo-drug and

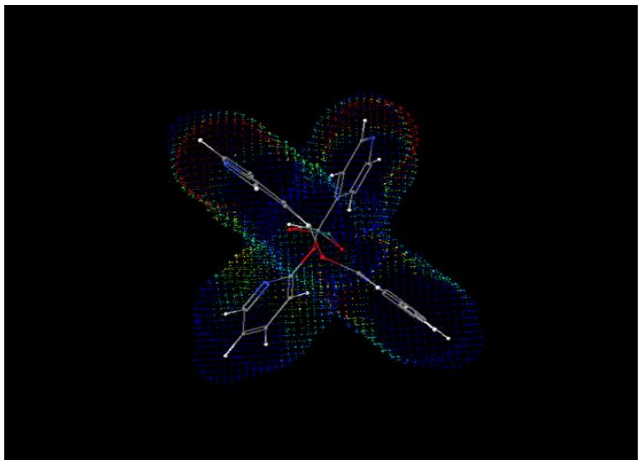

Figure 11: shows the shelled structure of the nano-composite system.

Table 1:

	Control (A375)	Complex(A375)	NT10(A375)	NT20(A375)	NT40(A375)	NCSNT (A375)	PN10 (A375)	PNS20 (A375)	PNS40 (A375)	NCSPNS (A375)
Cell Viability (% Control)	100	82	140	110	110	70	80	80	70	80
Cell Viability (% Control)UV	100	84	120	95	130	100	120	90	80	70

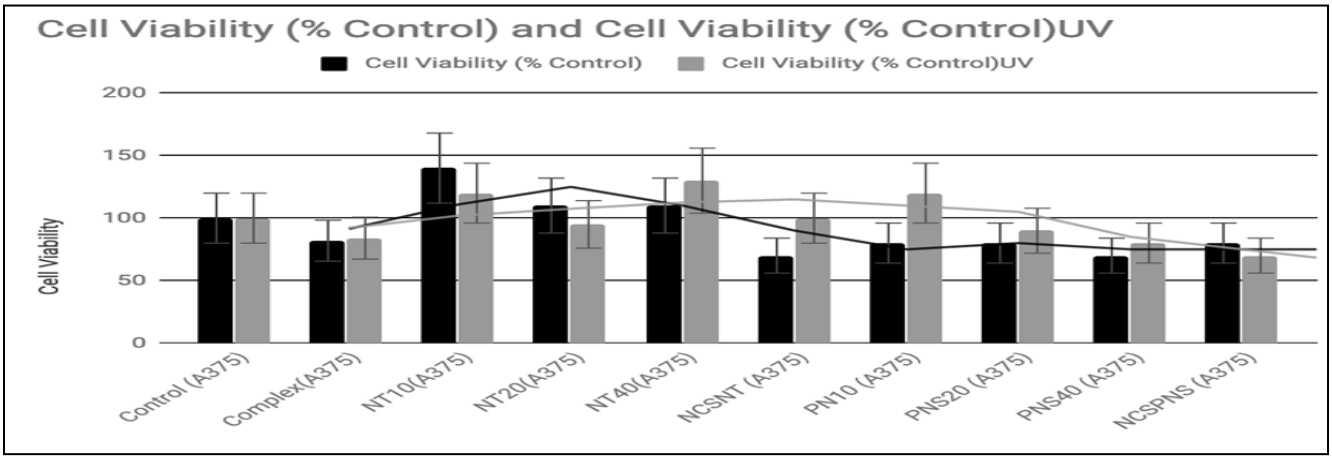

Figure 12:

Table 2:

Source of Variation	SS	df	MS	F	P-value
Between Groups	2962.666667	3	987.5555556	39.50222222	0.000038346642
Within Groups	200	8	25		
Total	3162.666667	11			

Table 3:

A	N	Mean	StDev	95% CI
Complex	3	90.67	5.77	(84.01, 97.32)
Control	3	100	0	(93.3, 106.7)
NCSNT	3	103.33	5.77	(96.68, 109.99)
NCSPNS	3	63.33	5.77	(56.68, 69.99)

Table 4:

	Control (SKBR3)	Complex(SKBR3	NT10(SKBR3)	NT20(SKBR3)	NT40(SKBR3)	NCSNT (SKBR3	PN10 (SKBR3)	PNS20 (SKBR3)	PNS40 (SKBR3)	NCSPNS (SKBR3
Cell Viability (% Control)	100	82	120	100	110	70	80	70	70	80
Cell Viability (% Control) and UV	100	94	90	75	130	110	120	90	100	60

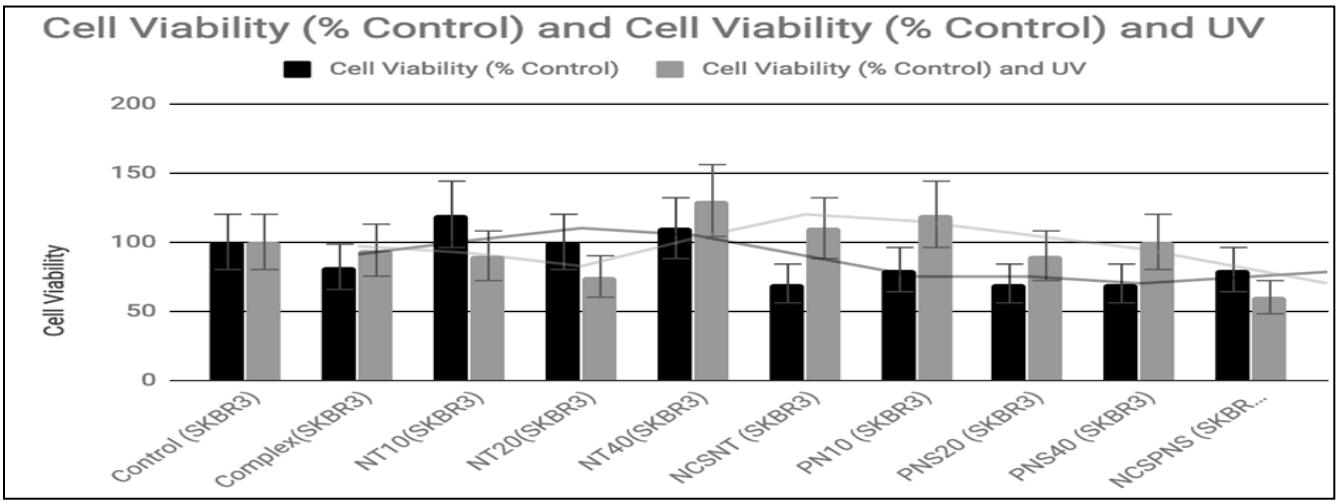

Figure 13:

Table 5:

A	N	Mean	StDev	95% CI
Complex	3	90.67	5.77	(84.01, 97.32)
Control	3	100	0	(93.3, 106.7)
NCSNT	3	103.33	5.77	(96.68, 109.99)
NCSPNS	3	63.33	5.77	(56.68, 69.99)

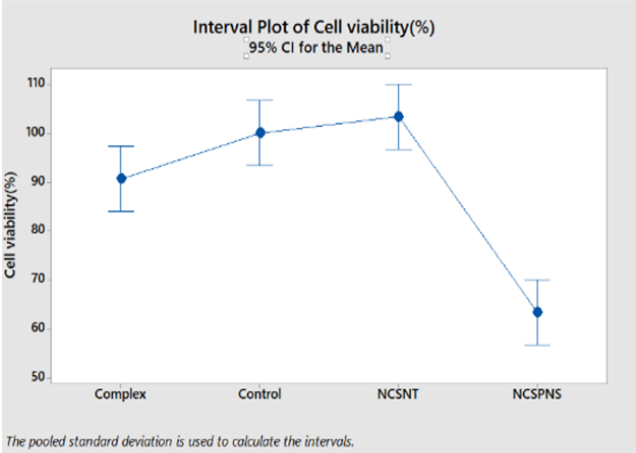

Figure 14:

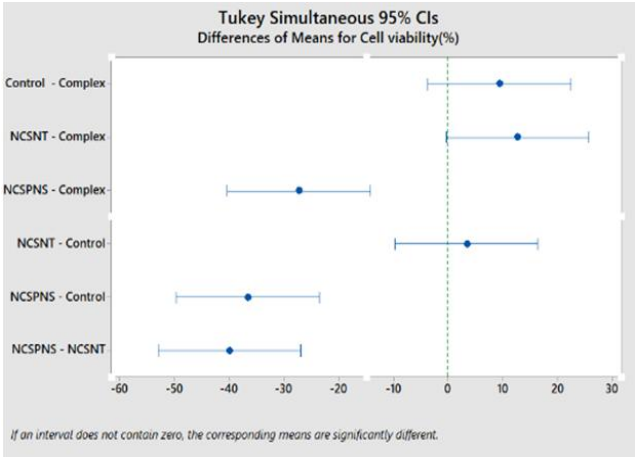

Figure 15:

Results and Discussion

The photo behaviour of metallo-drug complex was judged on the basis of maxima spectra, the spectra of the desired metallo-drug complex was used to confirm that the product of synthesis was not isomerized during sensitive synthesis. The size and shape of synthesised nanoparticles and structure of desired nanoparticles was determined by TEM. Lower Drug entrapment efficiency and loading efficiency compared to colloidal nanoparticles was estimated. Drug entrapment efficiency was estimated to (62±2)%, while the loading efficiency was (18.5±0.5)%. It is evident from the graphs obtained for cell viability that maximum cytotoxicity was obtained after UV illumination of cells treated with the PNSs loaded with Ru-complex that are represented by NCSPNS. However, the cytotoxicity was not much lower in comparison to control when the components were treated individually. The results are statistically significant at 0.05 level of significance with P-value 0.00003834 showing presence of difference in means. There existed significant difference between NCSPNS and control which was further verified by multiple comparison Tukey test.

Conclusion

This experiment represents an important step for optimization of usage of light for cancer treatment explained by photodynamic therapy. The results highlight PNSs as potential photosensitive carriers for metallo-drugs indicating lower cytotoxicity when compared to previous results obtained with colloidal nanoparticles. Stimulating effect in terms of cell growth was seen with SKBR3 and PANC1 cell lines as well. Further studies must be undertaken to determine the localization of the nanocomposite systems so as to get better understanding of the mechanism of their action and a deeper understanding of the type of tumors against which these systems would work most efficiently. On the basis of the obtained results for now, it can be speculated that the nanoparticles are mostly aggregated on the cell surface and cytotoxicity is due to oxidative stress mediated by reactive oxygen species

References

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