

# Development of Polymer Capped Sorafenib Loaded Gold Nanoparticles for Treatment of FLT3 Positive Acute Myeloid Leukemia

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## Leukemia

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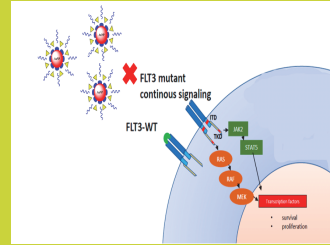
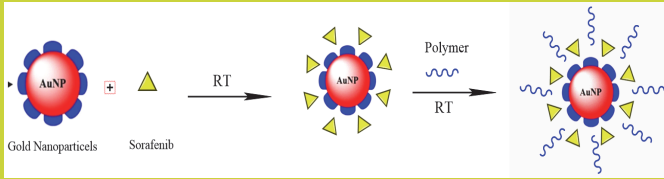
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## Purpose:

Development of sorafenib loaded PVP capped gold nanoparticles (GNP PVP Sot), physical characterization and cell studies.

Background: Sorafenib, a multikinase/FLT3 inhibitor, has shown its efficacy in AML+FLT3. Off-site side effects are the major limitation in continuous treatment [1, 2, 3].



## Methods:

Sorafenib loaded gold nanoparticles were characterized for drug loading and stability. Drug release profile was determined followed by determination of cytotoxicity potential in comparison to free drug and polymer capped gold nanoparticles.

## Results:

Sorafenib gold nanoparticles (GNP-PVP-Sot) were prepared by chemical synthesis. Drug loading was characterized by using <sup>19</sup>F NMR and HPLC. Drug release profile showed that 60 % of the drug was released in 4 hrs. Loading efficiency came out to be 13.3ug /mg of GNP's. Cell viability studies were done on AML (MV4-11) cell line.

Hemocompatibility was also determined.

### Physical Characterization

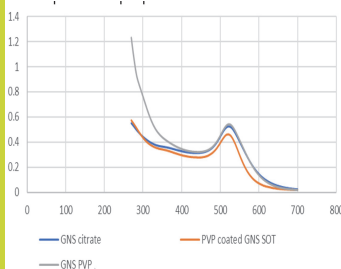


Fig.1, Surface Plasmon Resonance profile of gold chloride nanoparticles (GNPs), PVP functionalized gold nanoparticles (PVP-GNPs), Sorafenib loaded-PVP functionalized gold nanoparticles (GNS-PVP-Sots).

### FTIR spectra

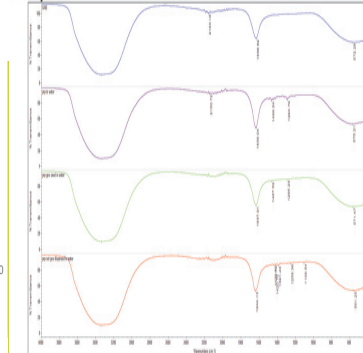


Fig.2, Fourier Transform Infrared spectra of gold nanoparticles (GNPs), poly vinyl pyrrolidone 10,000 (PVP), PVP functionalized GNP (PVP-GNP), sorafenib loaded PVP functionalized GNS (GNP-PVP-Sot).

## Quantification and Stability study

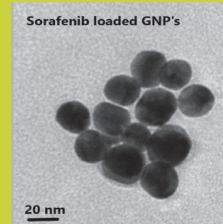


Fig 3. TEM of GNP-PVP-Sot

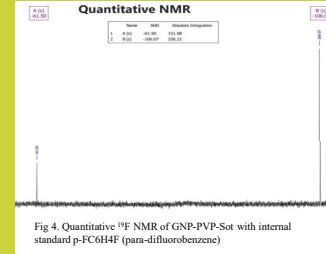


Fig 4. Quantitative <sup>19</sup>F NMR of GNP-PVP-Sot with internal standard p-FC6H4F (para-difluorobenzene)

	7 Days		14 Day		3 months		6 months	
	Size (nm)	PDI	Size (nm)	PDI	Size (nm)	PDI	Size (nm)	PDI
GNP'S	23	0.12	23	0.11	26	0.14	29	0.15
GNP-PVP	26	0.13	28	0.13	28	0.15	33	0.3
GNP-PVP-SOT	32	0.12	32	0.14	35	0.14	37	0.23

Table 1: Comparative data of Particle size and Polydispersity index of the prepared nanoparticles such as GNP, GNP-PVP, GNP-PVP-Sot at various time intervals, all formulations were stored in airtight container at 4 C and were sonicated for 2 min at room temperature before each measurement.

## Hemocompatibility and cytotoxicity study

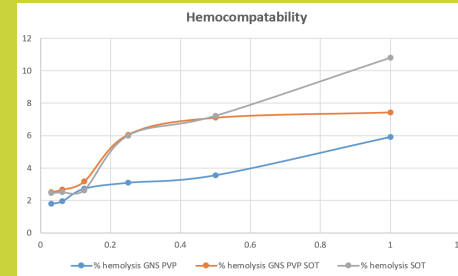


Fig 5 Hemolytic profile of GNP-PVP, GNP-PVP-Sot and free drug sorafenib tosylate (Sot)

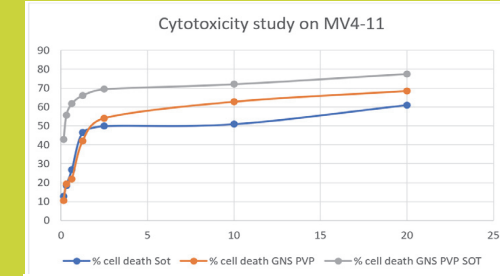


Fig 6 Cytotoxicity profile of GNP-PVP, GNP-PVP-Sot and free drug sorafenib tosylate (Sot)

**Conclusion:** The prepared nano formulation of sorafenib loaded and PVP capped gold nanoparticles showed promising characteristics for further studies on AML cells.

**References:** 1. Schroeder, T., et al., *Clinical Efficacy of Sorafenib in Patients with Acute Myeloid Leukemia (AML) and Activating FLT3-Mutations*. 2009, American Society of Hematology. 2. Liu, T., et al., *Sorafenib Dose Recommendation in Acute Myeloid Leukemia Based on Exposure-FLT3 Relationship*. Clinical and Translational Science, 2018. 11(4): p. 435-443. 3. Huang, X., et al., *Targeting Approaches of Nanomedicines in Acute Myeloid Leukemia*. Dose-response : a publication of International Hormesis Society, 2019. 17(4): p. 1559325819887048-1559325819887048.