A Computational Study of the Dissociation of CaS Nanoclusters in the Extracellular Fluid of Cancer Cells: The Effect of pH in the Structure and Stability of Protonated CaS Nanoclusters

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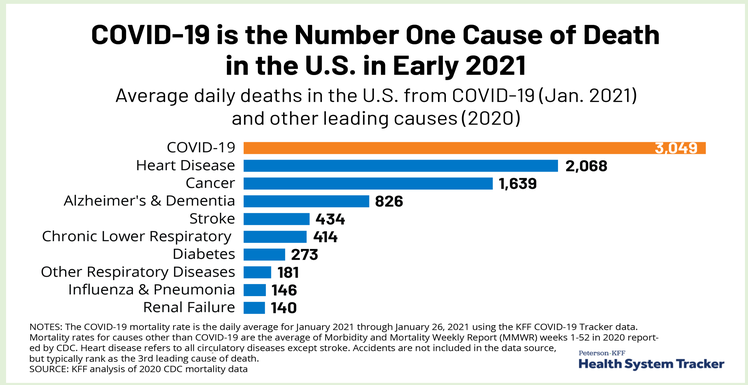
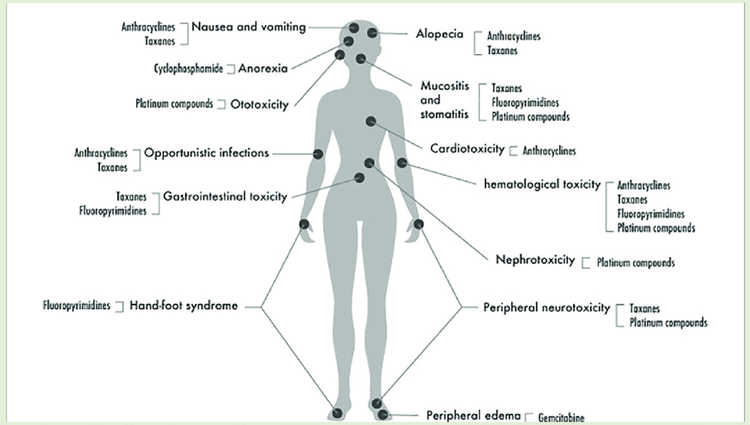
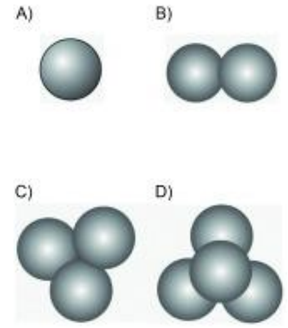
Significance



Leading causes of death in the US. Recovered from: https://www.kff.org/coronavirus-covid-19/slide/covid-19-now-leading-cause-of-death-in-the-united-states/.



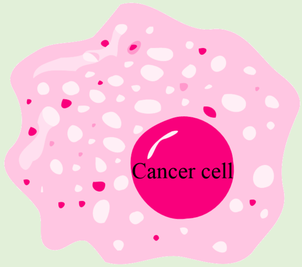
Chemotherapy side effects. Recovered from: Al-Mahayri, Z.; Patrinos, G.; Ali, B. Toxicity And Pharmacogenomic Biomarkers In Breast Cancer Chemotherapy. *Frontiers in Pharmacology* 2020, *11*.



Nanoparticles. Recovered from: Ellison, J.; Tschulik, K.; Stuart, E.; Jurkschat, K.; Omanović, D.; Uhlemann, M.; Crossley, A.; Compton, R. Get More Out Of Your Data: A New Approach To Agglomeration And Aggregation Studies Using Nanoparticle Impact Experiments. *ChemistryOpen* 2013, *2* (2), 69-75.

Innovation and Approach

- Previous work in the Castro lab showed CaS nanoclusters selectively caused cell death on malignant tumor cells.

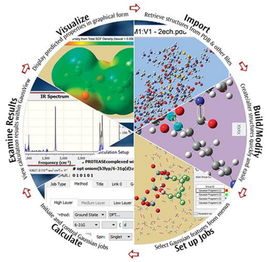


$pH_{extracellular}$ <7 (acidic)
Common and distinctive denominator of cancer cells

$$(CaS)_n \xrightarrow{2H^+} (CaSH_2)_n^{2+} \longrightarrow Ca^{2+} + H_2S$$

Ca^{2+}: Apoptotic agent (in cytosolic concentrations higher than 500nM)

H_2S: Genotoxic agent



GaussView 6. Recovered from: https://gaussian.com/gv6main/.

Approach

- DFT/B3LYP/DGVZVP level of theory of bare and protonated nanoclusters using Gaussian 16W and GaussView 6.0.16

Results

- Total cluster energy decreases with monomer units
- CaS monomer and dimer are more stable in water than in their standard state
- Protonation of the sulfur atoms increases the Ca-S bond length
- Protonation of the sulfur atom with 2 hydrogen atoms results in the formation of free calcium ions and hydrogen sulfide

Conclusions

- Protonation in acidic media increases the drive of dissociation into hydrogen sulfide and calcium ions
- CaS nanoclusters for selective inhibition of tumor growth with minimal impact to benign tissue

Future work

- Bond potential energy diagrams (bond dissociation energy)
- Calcium influx assays