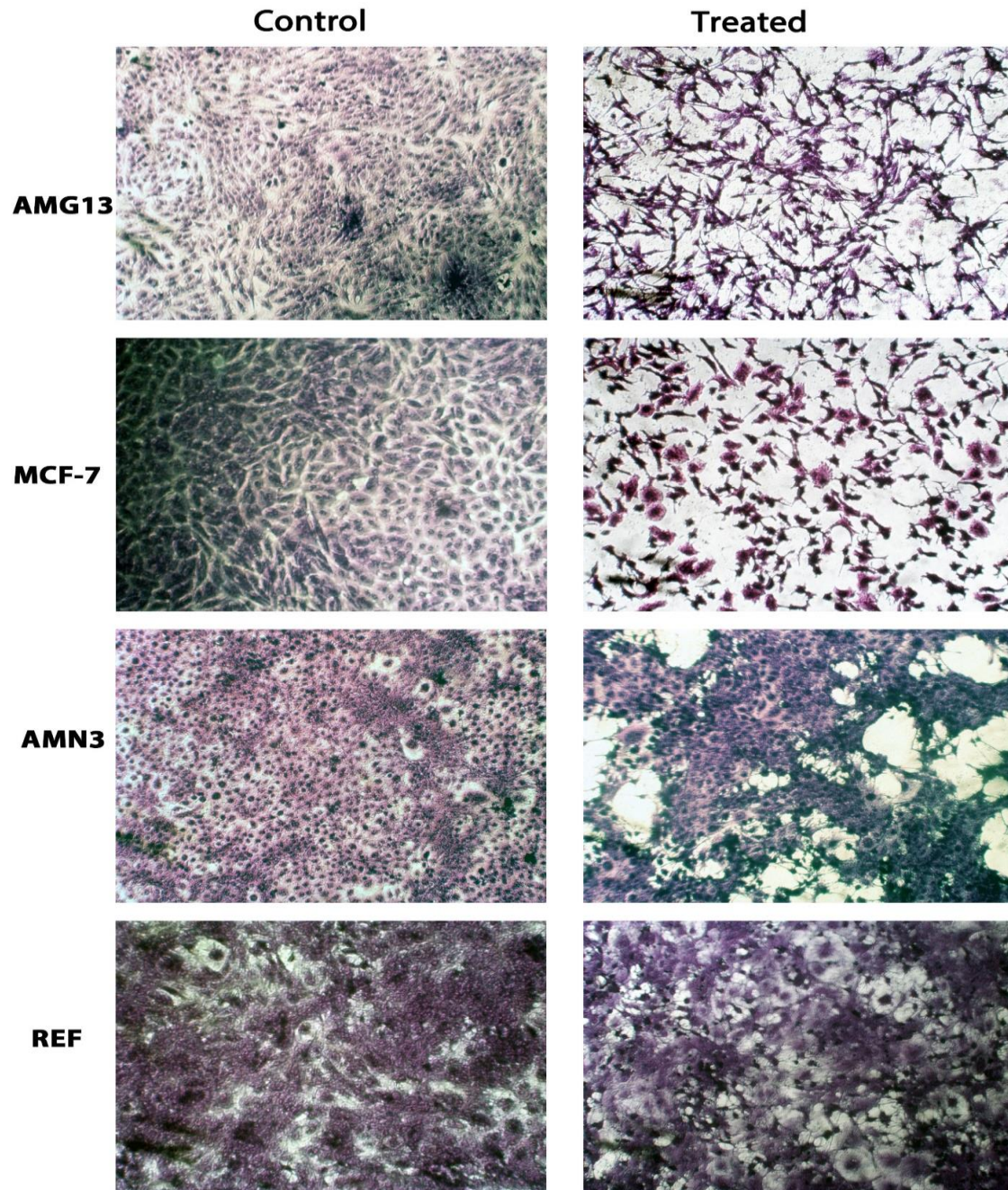
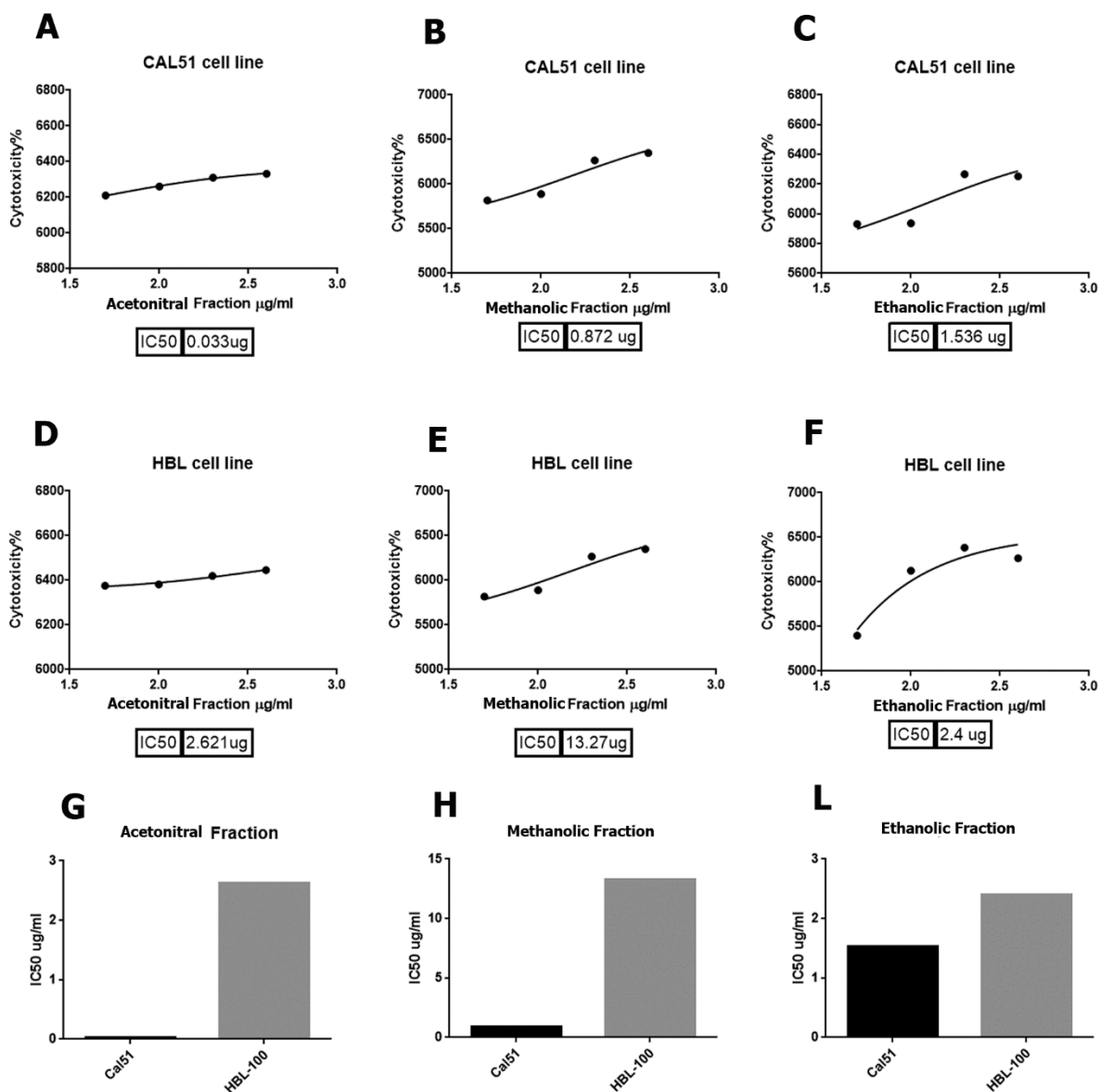


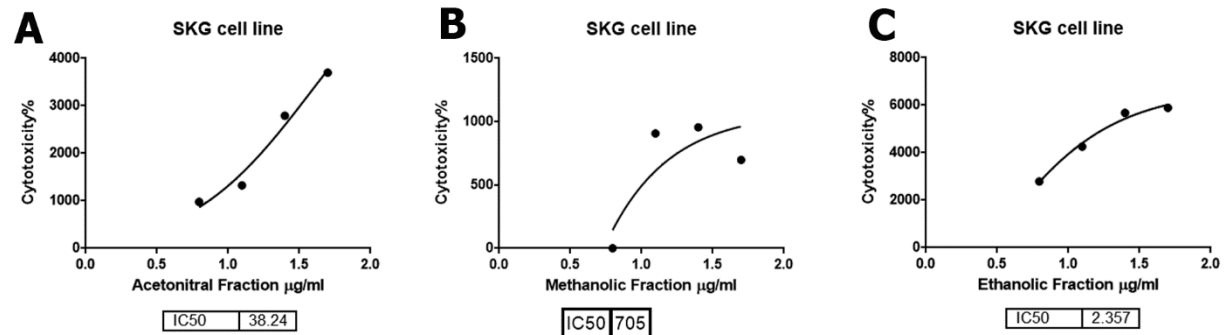
Supplementary Figure-7 indicated that most of the concentrations used effectively reduced the viability of cancer cells at higher doses while having nearly the same cytotoxicity in normal cells. Cv



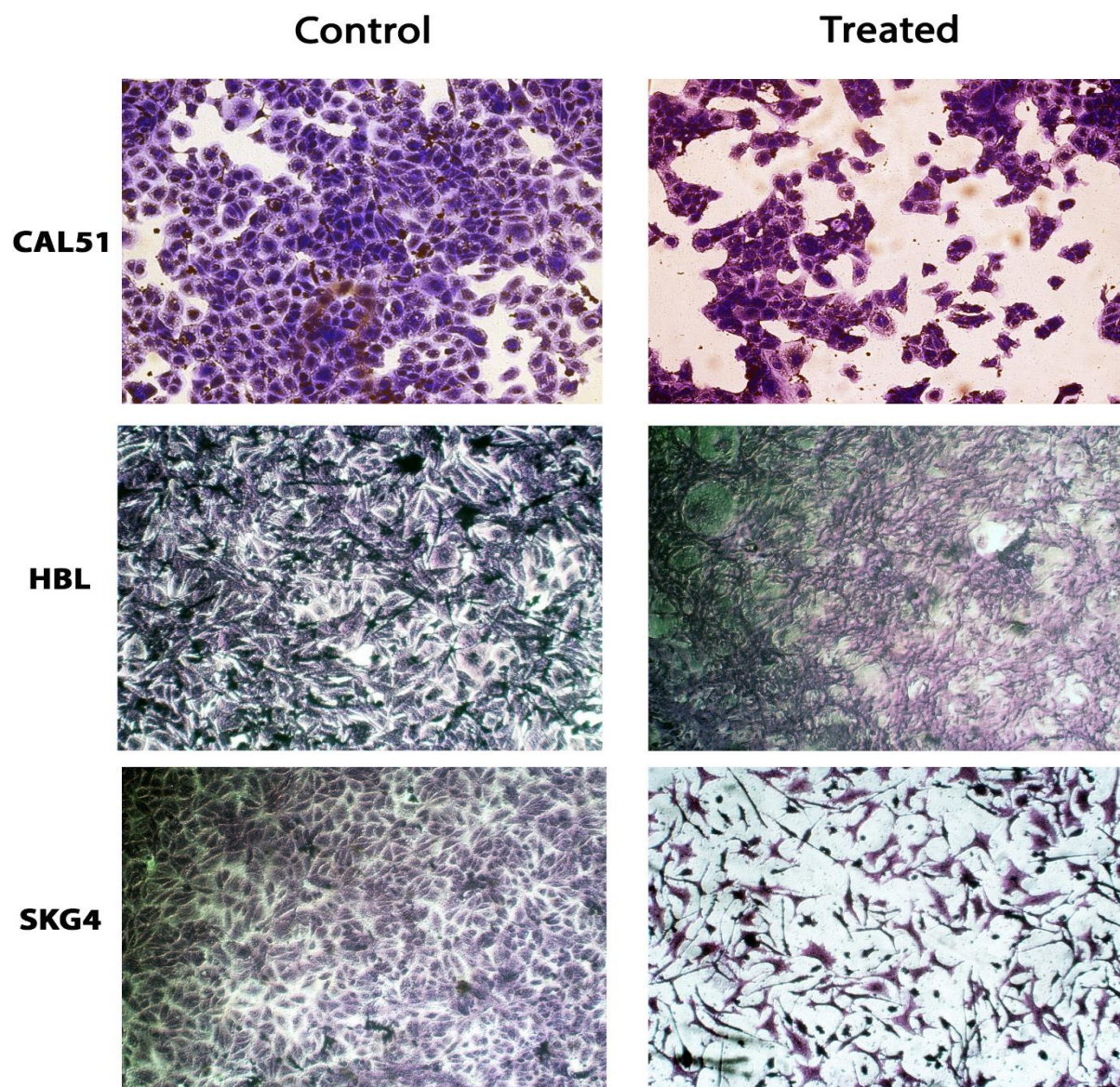
Supplementary Figure-8 cytopathological lesions in treated cells compared to untreated indicated cancer cells detachment, cytoplasmic and nuclear shrinkage, and cell rounding at IC50 dose of 125  $\mu\text{g}/\text{ml}$ . While having nearly the less cytotoxic effect in REF normal cells; however, there are also signs of cell detachment and shrinkage but in fewer numbers. Crystal violet staining, 400x.



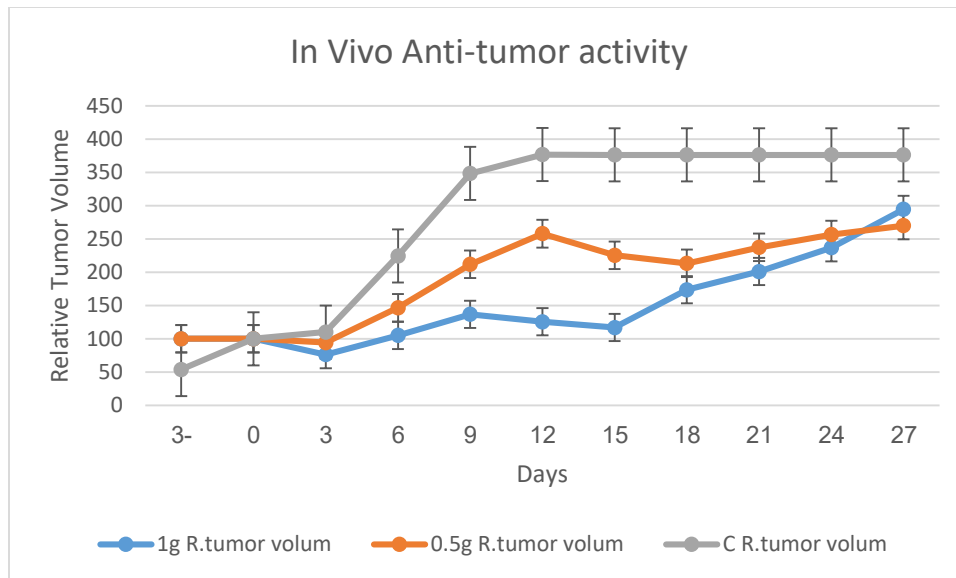
Supplementary Figure-9, cytotoxicity of the fractionated extract against normal and breast cancer cell lines. A) Acetonitrile fraction IC50 was 0.33 $\mu\text{g}$  in CAL51 cells. B) Methanolic fraction IC50 was 0.872 $\mu\text{g}$  in CAL51 cells. C) Ethanollic fraction IC50 was 1.536 $\mu\text{g}$  in CAL51 cells. D) Acetonitrile fraction IC50 was 2.621 $\mu\text{g}$  in HBL cells. E) Methanolic fraction IC50 was 13.27 $\mu\text{g}$  in HBL cells. F) Ethanollic fraction IC50 was 2.4 $\mu\text{g}$  in HBL cells. G) comparison between IC50 of acetonitrile fraction on cancer and normal cells showing the significant safety margin. H) comparison between IC50 of the methanolic fraction on cancer and normal cells showing the significant safety margin. L) comparison between IC50 of the ethanollic fraction on cancer and normal cells showing the high safety margin.



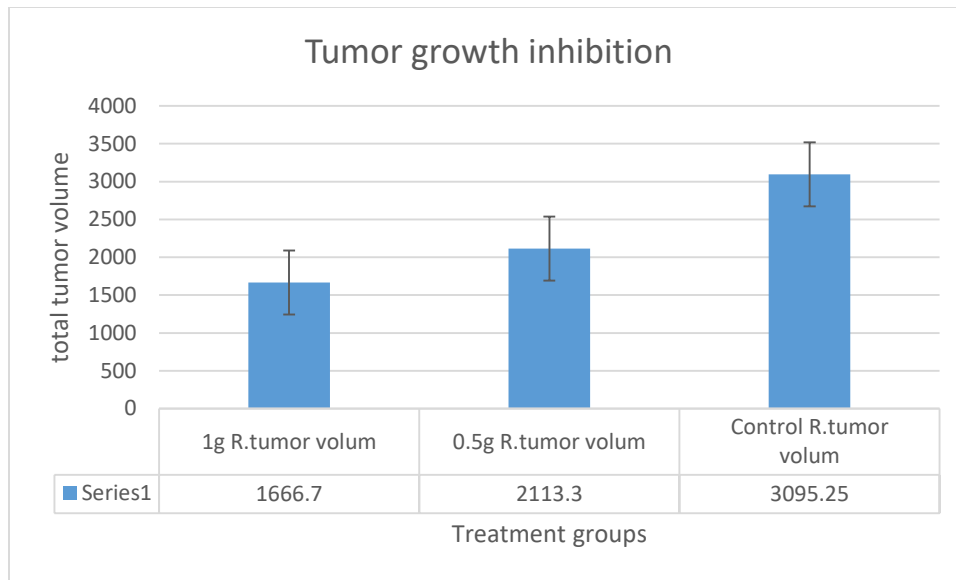
Supplementary Figure-10, cytotoxicity of the fractionated extract against human esophageal carcinoma cell lines (SKG). A) Acetonitrile fraction  $\text{IC}_{50}$  was 38.24 $\mu\text{g}$ . B) Methanolic fraction  $\text{IC}_{50}$  was 705 $\mu\text{g}$ . C) Ethanolic fraction  $\text{IC}_{50}$  was 2.357 $\mu\text{g}$ .



Supplementary Figure-11 shows the fractionated extract's cytopathological effect against normal and cancer cell lines. Acetonitrile fraction treated CAL51 breast cancer cells showed the most lesions at IC50 dose of 0.33ug compared to other fractions and untreated cancer cells. For the normal breast epithelial cells HBL, Ethanolic fraction showed the highest killing effect at IC50 dose of 2.4ug, mainly as cell detachment compared to untreated cells. Cytopathological lesions induced by the Ethanolic fraction at IC50 dose of 2.357ug were the highest when used to treat human esophageal carcinoma cell lines (SKG) compared to Acetonitrile fraction and Methanolic fraction and untreated cancer cells. Crystal violet staining. 400x.



Supplementary Figure 12, shows the relative tumor volumes displayed over a period of 30 days. The 1g/kg treatment group showed the greatest reduction of tumor growth in response to methanolic extracts of baked crab shell therapy ( $P < 0.05$ ).



Supplementary Figure 13. The group treated with 1g/kg showed a significant tumor growth inhibition rate by the end of the experiment.

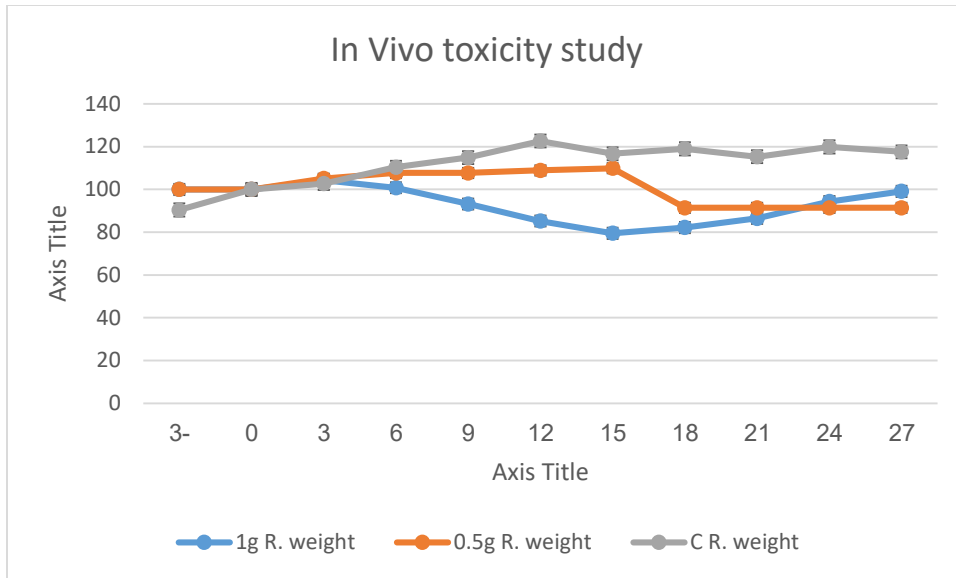


Fig. 14 showing the weight of the treated groups in compare to the untreated control group which shows no significant toxicity by the methanolic extract on mice weight even when using a high dose of 1 g/kg for 30 days