

THE UNIVERSITY OF TEXAS
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CANCER CENTER

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Dr. Leo Boulgak
Fersman Museum
Leninski pr.18, Building 2
Moscow, Russia 117071

Dear Dr. Boulgak:

I am happy to review for you as well as provide you with an update on the studies which we have conducted on your interesting compound, Astromelanin. Astromelanin appears to us to be a unique biopolymer with interesting properties certainly deserving further study.

Analysis: As you can see in the attached ion trace, we have performed an analysis of Astromelanin using a mass spectrometer. The data clearly indicate the polymer nature of the material with an average mass weight centered around 790 mass units. I have also attached the specific conditions (that is, instrument parameters) under which these analyses were performed.

Cytotoxicity: As we have previously discussed, Astromelanin is an active cytotoxic compound with interesting activity against human melanoma, breast, ovarian and colon tumor cell lines (studies performed in our laboratories here at M. D. Anderson Cancer Center). These studies consisted of incubating the cells for 72 hr with varying concentrations of Astromelanin prior to analyses of cell growth using the "MTT" assay. Although the concentrations of Astromelanin which inhibit cell growth of human cancer cells in culture are much higher than that of some of our more active anticancer drugs currently in use in the clinic, we have found that when Astromelanin is left in contact with cells over prolonged periods of time (for example up to 9 days) then the cytotoxicity resembles that achieved by standard anticancer compounds. This observation may in fact be providing us with a clue as to the potential mechanism of action of this compound and how it might be best used in the clinic. The data suggest that this compounds should be used at effective doses over a prolonged period of time perhaps as an infusion rather than single bolus doses separated by days or weeks.

Dr. Daniel Von Hoff, who is Head of the Institute for Drug Development, Cancer Therapy and Research Center in San Antonio, TX has also evaluated the cytotoxicity of Astromelanin for me at my request. He has found that against human HS578T breast cancer cells, Astromelanin produced complete inhibition of cell growth at concentrations of drug of 20 ug/ml and higher when cells were left in contact with drug for 6 days. Lower concentrations were not cytotoxic.

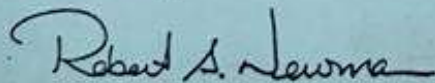
Toxicity/Antitumor activity: Our preliminary toxicology studies with, Astromelanin in mice have shown this compound to be relatively free from any major potential to injure the mice even when used on a daily basis for up to 7 days. Based on this information we have decided to proceed with several studies using mice with either hematologic tumors (leukemia) or solid tumors (Madison lung carcinoma). These studies are currently in progress.

Conclusion: This melanin biopolymer material has definite cytotoxicity against human cancer cells growing in culture and is therefore of interest. The preliminary toxicity studies indicate that the drug may also be a good candidate for further antitumor studies in mice and, in fact, these studies are currently underway.

In order for this material to make any further progress as a potential antitumor compound to be used one day in the clinic, much greater quantities of material are required and, of course, further preclinical studies are required. In addition, tests must be done to indicate that the same product is being produced each time (e.g. elemental analyses, mass spectrometry tests showing molecular weight distribution, etc.).

We continue to be interested in the development of this material. Please let us know if you are successful in obtaining funding to produce greater quantities of Astromelanin. We, in turn, will keep you informed of the studies we currently have underway with this interesting compound.

Sincerely,



Robert A. Newman, Ph.D.
Professor of Medicine