



Applications of TSC

Certain obstacles remain to the large scale implantation of Crocetin as a pharmaceutical for enhancing blood diffusivity in mammals, including humans. One problem is the preparation of the active agent in sufficiently pure and large amounts. Another, more serious problem is the fact that Crocetin is nearly insoluble in aqueous solutions, making preparation of a drug for intravenous administration particularly difficult. Finally, reaching and maintaining adequate levels of Crocetin to improve oxygen diffusivity, over a length of time, proves difficult.¹

Trans Sodium Crocetinate is the sodium salt of the trans-isomer of the carotenoid Crocetin with potential antihypoxic and radiosensitizing activities.

Trans Sodium Crocetinate (TSC) increases the diffusion rate of oxygen in aqueous solutions such as from plasma to body tissue.²

TSC improves the diffusion of oxygen and glucose, and increases oxygenation in ischemic brain tissue and dampens the intensity of an ischemic challenge during an ongoing ischemic event, that may occur in hemorrhage, vascular and neurological disorders, and in the tumor microenvironment.^{3 2}

Adjuvant treatment with radiation (radiation therapy or radiosurgery) is a mainstay of treatment for patients harboring glioblastomas multiforme (GBM). Hypoxic regions within the tumor make cells less sensitive to radiation therapy. Trans Sodium Crocetinate (TSC) helps to increase oxygen diffusion in the brain and elevate the partial brain oxygen level.⁴

¹ [John L. Gainer](#), Trans-sodium crocetin, methods of making and methods of use thereof

² <https://pubchem.ncbi.nlm.nih.gov/>

³ Trans-Sodium Crocetin Improves Outcomes in Rodent Models of Occlusive and Hemorrhagic Stroke
[Yi Wang](#), [Ryo Yoshimura](#), [Hiroaki Manabe](#), [Catherine Schretter](#), [Ryon Clarke](#), [Yu Cai](#), [Mark Fitzgerald](#), and [Kevin S. Lee](#),

⁴ Jason Sheehan, Adina Ionescu, Nader Pouratian, D. Kojo Hamilton, David Schlesinger, Rod J. Oskouian Jr., Charles Sansur, "Use of trans sodium crocetin for sensitizing glioblastoma multiforme to radiation"



The company behind the research is Diffusion Pharmaceuticals which is studying related carotenoids as well:

OVERVIEW / TRANS SODIUM CROCETINATE (TSC)

A successful Phase 1/2 trial of TSC in newly diagnosed GBM patients was completed in 2015 by Diffusion Pharmaceuticals. Subsequently, agreement was reached with the Food and Drug Administration (FDA) on the design of a single Phase 3 study that would support registration of TSC for the treatment of newly diagnosed GBM patients, in combination with radiation and/or chemotherapy. Discussion is currently underway with the regulatory authorities regarding design of a clinical development program in pancreatic cancer. Trials in brain metastasis are in the planning stages, with enrollment expected following interim results in the pancreatic cancer study. TSC has received Orphan Drug Designation for the potential treatment of GBM and brain metastasis, and expects to receive Orphan Drug Designation for pancreatic cancer in the near future.⁵

CLINICAL TRIAL RESULTS

In 2015, Diffusion Pharmaceuticals completed a Phase 1/2 study of Trans Sodium Crocetin (TSC) in 59 patients with newly diagnosed primary brain cancer (GBM). The results demonstrated that people who received TSC plus radiotherapy and temozolomide chemotherapy benefited from a substantial improvement in overall survival (OS) compared to the historical control group who received radiotherapy and temozolomide chemotherapy alone.

TSC plus radiotherapy and chemotherapy increased the patients' chance of survival at two years by 37 percent compared to the historical control. In the subgroup of patients considered inoperable, the chance of survival at two years for those who received TSC was increased almost 4 fold. No negative safety findings were observed in the TSC GBM study and no serious adverse events were attributed to TSC in any patient.⁵

⁵ <http://www.diffusionpharma.com>



TSC GBM CLINICAL STUDY RESULTS EXAMPLE OF COMPLETE TUMOR REGRESSION -- PATIENT 427

