Silibinin Summary for Intravenous use

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INTRAVENOUS SILIBININ:

Silymarin intravenous compounds have the potential for multiple mechanisms of action in the oncology and chronic illness setting. Silibinin the intravenous form appears, from our clinical experience, to be potent and helpful in these settings. It is however a less stable parenteral product and requires special handling and administration.

INTRAVENOUS USE GUIDELINES:

Dose:

- Test dose at 75 mg IV on the first day [1]
- Subsequent doses could increase to 150 to 300 mg if tolerated two to three times weekly [1].

Administration:

- Intravenous dosing via either a central or peripheral line.
- Carrier solutions: Defer to compounding pharmacy.
    - Dextrose 5% in Water (D5W) 100 to 500 mL carrier solution
    - 0.9% normal saline (NS) 100 to 500 mL carrier solution
- Rate of administration: 45 to 90 minutes as tolerated by the patient for 100 ml solution
    - Monitor for signs of non-anaphylactic detoxification reaction including itching, shaking, flushing, headache. Treat with fluids and oxygen. [1]
    - For allergic / anaphylactic reaction treat per standard protocol.
- Other IV compatibility:
    - Acceptable in series with IV antioxidant and other nutrient formulas
    - Do not mix in the same bag with any other IV solutions.
        - Sodium bicarbonate may be needed to buffer pH once product is in the IV bag.
        - pH of product tends to be alkaline for storage and shipping
- Other IV incompatibility:

- Avoid oxidative therapies like high dose ascorbate and Silibinin on the same day.

Screening:

- Intolerance to oral silymarin compounds is a caution and may exclude use in the IV setting
- Lab studies:
    - CBC, Chemistry panel (Metabolic panel including electrolytes, bilirubin, AST/ALT/GGT, eGFR/BUN/CRE).

Cautions:

- Silibinin can cause rapid hepatic reactions resulting in the transient but profound non-anaphylactic "detoxification" reactions listed above. These reactions may be due to SNP's in the GST, SOD or other areas but this is only conjecture at this point. So while doses far above 150-300 mg have been suggested it is best to assure patient tolerance of lower doses prior to administration.

SELECTED LITERATURE SUMMARY:

(Bold emphasis added by the reviewer)

Abstract: (Comelli)
The protective effects of silymarin and silibinin, demonstrated in various tissues, **suggest a clinical application in cancer patients as an adjunct to established therapies, to prevent or reduce their toxicity.** Here we discuss the possible mechanism of the **protective action of silymarin and silibinin**, focusing on cancer therapies as agents causing cellular damage.

Abstract: (Ramasamy)

Silymarin modulates imbalance between cell survival **and apoptosis through interference with the expressions of cell cycle regulators and proteins involved in apoptosis. In addition, silymarin also showed anti-inflammatory as well as anti-metastatic activity. Further, the protective effects of silymarin and its major active constituent, silibinin, studied in various tissues, suggest a clinical application in cancer patients as an adjunct to estabilished therapies, to prevent or reduce chemotherapy as well as radiotherapy-induced toxicity.** This review focuses on the chemistry and analogues of silymarin, multiple possible molecular mechanisms, *in vitro as well* as *in vivo anticancer activities, and studies on human clinical trials.*

Abstract: **(Kaur)**

***Apart* from chemopreventive effects, other noteworthy aspects of silymarin and its active constituent silibinin in cancer treatment include their capability to potentiate the efficacy of known chemotherapeutic drugs, as an inhibitor of multidrug resistance associated proteins, and as an adjunct to the cancer therapeutic drugs due to their organ-protective efficacy specifically liver, and immunostimulatory effects.** Widespread use of silymarin for liver health in humans and commercial availability of its formulations with increased bioavailability, further underscore the necessity of carrying out controlled clinical trials with these agents in cancer patients. In this review, we will briefly discuss the outcomes of clinical trials being conducted by us and others in cancer patients to provide insight into the clinical relevance of the observed chemopreventive effects of these agents in various epithelial cancer models.

Abstract: **(Vaid)**

Changes in life style over the past several decades including much of the time spent outdoors and the use of tanning devices for cosmetic purposes by individuals have led to an increase in the incidence of solar ultraviolet (UV) radiation induced skin diseases including the risk of skin cancers. Solar UV radiations are considered as the most prevalent environmental carcinogens, and chronic exposure of the skin to UV leads to the squamous and basal cell carcinoma and melanoma in human population. A wide variety of phytochemicals have been reported to have substantial anti-carcinogenic activity because of their antioxidant and antiinflammatory properties. Silymarin is one of them and extensively studied for its skin photoprotective capabilities. Silymarin, a flavanolignan, is extracted from the fruits and seeds of milk thistle (***Silybum marianum L. Gaertn.), and has been shown to have*** **chemopreventive effects against photocarcinogenesis** in mouse tumor models

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References:

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4. Kaur M and Agarwal R. Silymarin and Epithelial Cancer Chemoprevention: How close we are to bedside? Toxicol Appl Pharmacol. 2007 November 1; 224(3): 350–359. doi:10.1016 /j.taap.2006.11.011.

5. Vaid M and Santosh K Katiyar SK. Molecular mechanisms of inhibition of photocarcinogenesis by silymarin, a phytochemical from milk thistle (Silybum marianum L. Gaertn). Int J Oncol. 2010 May; 36(5): 1053–1060.