

# Teratogenicity of the Solanum Alkaloid Solasodine and of 'Kennebec' Potato Sprouts in Hamsters

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In the course of studies concerned with the teratogenic effects of certain naturally occurring plant compounds, we have investigated the teratogenicity of steroidal alkaloids derived from the plant *Veratrum californicum* (KEELER and BINNS, 1966; KEELER, 1969 and 1970a). These trials established that fetal rats, rabbits, hamsters and sheep were susceptible only to those veratrum alkaloids that have a terminal furanopiperidine group (KEELER, 1968, 1970a, 1970b, 1975a).

More recently, we have investigated the potential teratogenicity of similar steroidal solanum alkaloids derived from plants of the solanum genus. Based on our experience with the veratrum alkaloids, we considered it probable that teratogenic effects in mammals from the solanum group of alkaloids, if any occurred, would be associated with the spirosoles. The spirosoles also possess terminal furan and piperidine rings and have certain structural and configurational similarities to the teratogenic veratrum alkaloids (KEELER, 1973).

The spirosole alkaloid, solasodine, was found to be non-teratogenic in rats (KEELER, 1973). However, in subsequent tests solasodine has produced teratogenic effects in hamsters when administered at considerably higher doses than those given to rats. When 120 g bred hamsters were gavaged once on day 7 or 8 of gestation with solasodine suspended in 3 cc of H<sub>2</sub>O, the compound produced 48 deformed offspring in 23 of 89 (25.8%) litters from surviving pregnant dams. One hundred eighty mg was the usual dose. Day 1 of gestation was considered to begin at midnight preceding the finding of sperm on morning vaginal lavage.

Deformities produced were grossly categorized as exencephaly, cranial bleb, and spina bifida, each occurring with about equal incidence. Exencephalics had disproportionately small and malformed heads with a prominent dorsocranial defect that exposed a contused but otherwise normal brain. Exposure commonly extended from the frontal poles of cerebral hemispheres to caudal mesencephalic

tectum, and often included the median parts of the immature cerebellum. Organic components of the brain appeared histologically to be normally differentiated. The mesencephalic flexure was commonly exaggerated. Cranial blebs consisted of soft protuberances and discolorations of skin in the interparietal midline overlying compressed or contused brain and meningeal tissues, and apparently represented mild or incipient forms of exencephaly. Spina bifida fetuses had protuberances of skin and other soft tissues in the dorsal midline of the lumbosacral region, with herniation of cord tissues from the vertebral canal to a subcutaneous location. Histologically, the lesion varied in severity; mild forms were related to absence or dysplasia of mesenchymal components of vertebral arches or to their delayed chondrification; in severe forms, vertebral centra of the affected region were misaligned or even absent. Tissues of the cord itself were commonly not abnormal.

We have also tested the teratogenicity in hamsters of potato sprout preparations from a cultivar reported to contain a high content of spirosolane-type alkaloidal glycosides (KUC, 1973). The preparations were air dried, ground sprouts of the 'Kennebec' potato (no tuber material included). Potatoes were sprouted by washing the tubers and leaving them at room temperature while covered with black cloth. Sprouts were harvested when they averaged 2.5-5 cm in length, and immediately dried at 30° C in a current of air, ground, and stored at room temperature. When gavaged to bred hamsters once on gestation days 7, 7 1/2, or 8 at 500 mg, these sprout preparations produced 64 abnormal offspring in 26 of 113 (23%) litters from surviving, pregnant dams. The deformities included exencephalics, spina bifidas and cranial blebs grossly similar to those described, and, additionally, microphthalmia. Nearly 80% were exencephalics and blebs while microphthalmics or spina bifidas were less common. We have not determined as yet whether the grossly similar defects from solasodine and from sprout gavage are comparable histologically.

Collectively, 183 control hamsters either gavaged with water carrier alone or non-gavaged produced only 3 litters (1.6%) with single abnormalities, and only 1 of the 3 abnormal fetuses (an exencephalic) was of a type seen in treated animals. Gavage with either solasodine or sprout preparations significantly increased resorptions over control levels.

RENWICK (1972) advanced an hypothesis that potato avoidance by pregnant women would reduce incidence of human congenital spina bifida and anencephaly by 95% in certain areas. He suggested that the potato alkaloids, among other possibilities, could be the teratogens. Subsequent potato avoidance trials by others caused him to

abandon this optimistic hypothesis (RENWICK, 1974). While studies on the toxicity and to an extent the teratogenicity of solanum alkaloids have been widely reported, none have been specifically concerned with the teratogenicity of the spirosolanes.

We have not yet identified the teratogen nor its compound class from the 'Kennebec' sprouts and do not know, therefore, whether it is a spirosolane. Neither solasodine nor its glycosides have been isolated, to our knowledge, from potatoes, but other spirolanes have been. These spirosolanes are configurationally different in the piperidine ring (SCHREIBER, 1968). Preliminary data suggest that 'Kennebec' tuber material is not teratogenic at doses four times as high.

#### ACKNOWLEDGMENTS

This research was supported in part by an inter-agency agreement between the U.S. Department of Agriculture, Agricultural Research Service, and the National Institutes of Health, National Institute of General Medical Sciences as funded by the latter.

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