When administered systemically in another study, however, various drugs dissolved in DMSO did not differ significantly in their lethality or cellular pene-
tration as compared to the same drug administered in saline (34). Intravenous doses of 50% DMSO in rabbits produced no adverse effects other than a transient fall in blood pressure, which was reversible (30).

The absorption of phenylbutazone dissolved in an aqueous solution of DMSO was rapid and complete after oral administration (38). Alcohol used to dissolve the drug was not improved using the subsutaneous route simultaneously with DMSO.

However, phenylbutazone could be detected in the rabbit's blood for several hours after an oral administration containing DMSO and 5% phenylbutazone was applied to the skin. This was due to the fact that the drug diffusion rate increased in DMSO containing solutions. An increase of phenylbutazone in the muscle tissues underlying the site of application over a control containing phenylbuta-
zone alone was observed in a previous study (38).

When 1% fluorescein was injected intradermally at several different concentra-
tions of DMSO in man, the dermal clearance of this substance was considerably decreased relative to that in control skin (29).

This was due to reduced diffusion through the dermis (29).

The addition of 50% DMSO to solutions containing 1% old tuberculin (OT) abolished positive patch test reactions in tuberculin sensitive human subjects, and 50% DMSO also prevented the dermals from producing 1% by 1% (38). A similar protective effect has been shown in a previous study (29).

DMSO has to some extent neutralized the toxic effects of certain proteins causing their denaturation (28). DMSO has also been reported to alter the properties of proteins in certain instances (28).

In the human, DMSO did not exert any beneficial effects on experimentally induced thermal burns, contact dermatitis or ultraviolet burns. It was noted in this study that burn injuries improve when a restraint is applied (29).

In experimentally induced thermal edema of the legs of rabbits, the leg volume was significantly reduced through the use of DMSO. This effect could be markedly reduced by the hourly application of undiluted DMSO to the injured legs (35).

In the human, DMSO did not affect the viability of cultured mammalian cells in vitro, where their irritant actions could be displayed. When DMSO was used clini-

cally, it was shown to cause erythema and blistering. For this reason, DMSO Solution at a total daily dose of 20–40 mL administered topically for 21 consecutively.

In rabbits the application of 70% DMSO, adjacent to but not on the wound incision site, appeared to increase the development of wound tensile strength.

A compilation of the results for a number of acute toxicity (LD₅₀) determinations demonstrated the toxicity of DMSO (32, 33, 34) in several experi-

mental animal species as is follows:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rd. of Administ</th>
<th>LD₅₀ (g/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>IP</td>
<td>16.0 – 20.5</td>
</tr>
<tr>
<td>Mouse</td>
<td>IP</td>
<td>13.621 – 28.3</td>
</tr>
<tr>
<td>Dog</td>
<td>IP</td>
<td>2.5 – 12.5</td>
</tr>
<tr>
<td>Guinea pig</td>
<td>IP</td>
<td>16.0</td>
</tr>
<tr>
<td>Human</td>
<td>Oral</td>
<td>13.9 – 20.5</td>
</tr>
<tr>
<td>Rat</td>
<td>Oral</td>
<td>16.0 – 20.5</td>
</tr>
<tr>
<td>Mouse</td>
<td>Oral</td>
<td>15.0 – 22.0</td>
</tr>
<tr>
<td>Dog</td>
<td>Oral</td>
<td>16.0 – 20.5</td>
</tr>
<tr>
<td>Guinea pig</td>
<td>Oral</td>
<td>2.5 – 12.5</td>
</tr>
</tbody>
</table>

In rabbits the application of 70% DMSO, adjacent to but not on the wound incision site, appeared to increase the development of wound tensile strength over controls (48).

The intravenous concentration of DMSO resulted in an increasing inhibition of fibrinolysis, in vitro, which was reversible (39). There was also a decrease in fibrinogen levels following the dermal or systemic administration of DMSO, and a transient doubleing of urine volume after the intravenous administration of the drug (48).

DMSO has been shown to have a low toxicity when repeated oral administra-
tion in rats, which was reversible (30). It is believed that, similar to chelating agents, DMSO has the ability to produce neuronic toxicity due to irreversible damage to the stratum corneum (28).

The Schwartzman reaction (30). It is believed that, similar to chelating agents,

DMSO alone is also a strong irritant, causing only a transient hypotension and apnea was no longer observed. Repeated intravenous doses in the rat and cat resulted in a transient lowering of blood pressure and blood glucose levels. This effect was also shown to carry physostigmine and phenylbutazone through the skin of the rat and cat (48).

No significant hematologic or biochemical changes were noted in rats is not affected by the intravenous administration of 100 mg DMSO/100 g body weight during 3 days (22).

DMSO treatment administered intraperitoneally to rats for 30 days decreased experimental pulmonary fibrosis induced by bleomycin, increasing lung dry weight to saline, cortisone acetate or a combination of cortisone and DMSO admin-
distered at 40 mg/kg. (48).
in a variety of experimental animals including rats, dogs, swine, rabbits and humans. Following oral or topical administration of DMSO, certain eye changes have been observed. These effects are temporary and are not considered to be of serious nature. Upon topical application, they are self-limiting reversible states, and not necessarily an indication to discontinue therapy.

DOMOSO Solution should not be used under occlusive dressings. DOMOSO Solution is a potent solvent and may have a deleterious effect on the skin, mucous membranes and other tissues. If irritation develops, DOMOSO Solution should not be used until irritation subsides. In general, adverse reactions are local, and while they may prove to be annoying to some patients, they are usually not of a serious nature. Upon topical application, they are self-limiting reversible states, and not necessarily an indication to discontinue therapy.

DOMOSO Solution should not exceed 30 days. Horses — Liberal application should be administered two to three times daily.

DIABETES MELLITUS

DOMOSO Solution may mask certain disease signs such as are seen in diabetes mellitus. DOMOSO Solution should not be used directly prior to racing or other physical stress wherein the drug might mask existing pathology, such as a fracture. These effects are temporary and are not considered to be of serious nature. DOMOSO Solution should not be used under occlusive dressings. DOMOSO Solution is a potent solvent and may have a deleterious effect on the skin, mucous membranes and other tissues. If irritation develops, DOMOSO Solution should not be used until irritation subsides. In general, adverse reactions are local, and while they may prove to be annoying to some patients, they are usually not of a serious nature. Upon topical application, they are self-limiting reversible states, and not necessarily an indication to discontinue therapy.

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