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Clinical Study Shows Glucosol™ Is Effective in Reducing Blood Glucose Levels

Study Objective

In 1999 a clinical study was conducted by Dr. William V. Judy at the Southeastern Institute of Biomedical Research, Bradenton, Florida, to confirm Corosolic acid's effect in lowering blood glucose levels and to evaluate dose-response relationship.

In a recent randomized, double-blind, cross-over clinical study conducted over four months in Florida, the active ingredient of Glucosol,™ Corosolic acid, is effective in reducing blood glucose levels, with no signs of adverse effects.

Study Subjects

This randomized, double-blind, cross-over trial was conducted with 12 subjects (6 men and 6 women) over 22 weeks. An initial dose-response trial was conducted on a group of 10 subjects (5 men and 5 women).

The criteria for including subjects in this study were mild case insulin independent diabetes (Type II), inability to tolerate glucose burden, glucose levels of more than 150 mg/deciliter (fasting level) and subjects older than 46 years of age with an informed consent. The clinical reference value of normal blood glucose ranges from 65 to 110 mg/deciliter.

Dose-Response Relationship

To evaluate the response of the patients to different dose levels and different formulations of Glucosol,™ it was given orally according to the following regimen:

The ten subjects were divided into two groups of five. Both groups were given orally a placebo for two weeks. Following the placebo period, one group was given orally an oil-based soft gelatin capsule and another group was given a powder-based two-piece hard gelatin capsule. Each capsule (two-piece or soft gelatin capsule) contained 8 mg Glucosol™. The initial dosage regimen was 16 mg Glucosol™ daily for two weeks. Fasting glucose levels were measured in venous blood at 15 and 30 days of Glucosol™ supplementation. The dose of Corosolic acid, the active ingredient of Glucosol,™ was 1.0% or 0.16 mg/day. A (placebo) washout period of 2 weeks was allowed before beginning the next dosage regimen on both groups. The second dosage regimen was 32 mg Glucosol™ per day. Again, a 2 week (placebo) wash out period was allowed before the last dosage regimen. The last dosage was 48 mg Glucosol™ per day.

The average fasting blood glucose level in both groups during placebo treatment was 167.5 mg/deciliter.

Glucosol™ formulated in an oil base in soft gelatin capsules were given to each group of five people at 16 or 32 or 48 mg Glucosol™ per day for 2 weeks. The average blood glucose level dropped 4.9% at 16 mg Glucosol,™ while the decrease was 10.7% at 32 mg Glucosol,™ and a

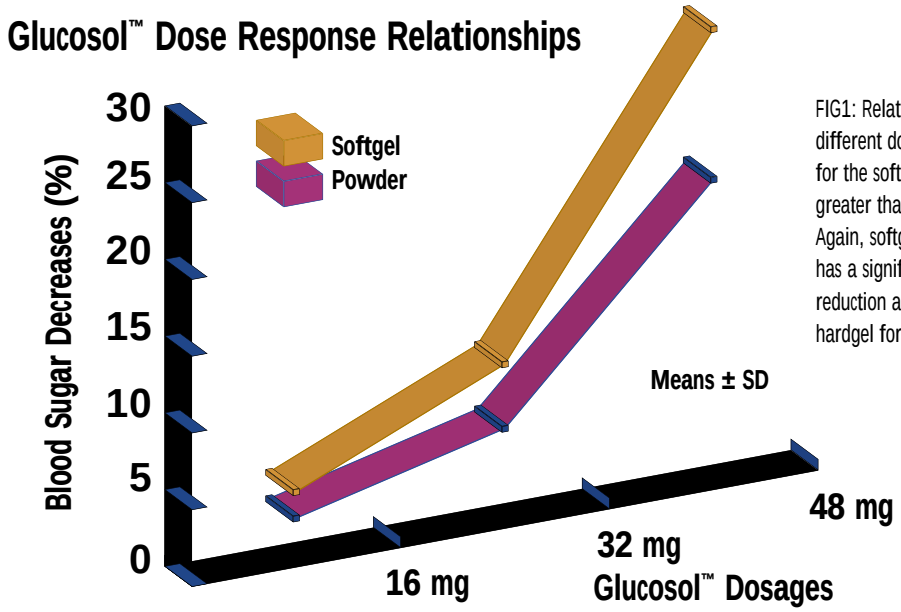

FIG1: Relative changes in blood sugar content with different dosages of Glucosol™. Note that changes for the softgel formulation is significantly ($p>0.001$) greater than that for the hardgel formulation. Again, softgel formulation with Glucosol™ extract has a significantly greater effect on blood sugar reduction at a dose of 48 mg than does that for the hardgel formulation.

drop of 31.9% was noted at 48 mg Glucosol™ dose per day (Figure 1).

The second group of five people were given Glucosol,™ formulated in a dry powder base in two-piece hard gelatin capsule, at 16, 32 or 48 mg Glucosol™ per day. In this group, compared to the placebo, the average blood glucose level dropped by 3.18% at 16 mg Glucosol,™ 6.5% at 32 mg Glucosol,™ and 20.2% at 48 mg daily dose of Glucosol™ (Figure 1).

These results indicate that the higher the daily dose of Glucosol,™ the greater the drop in blood glucose levels.

Further, an oil-based soft gelatin capsule formulation of Glucosol™ seems to be more potent than a comparable dry-powder formulation of Glucosol™ in a two-piece hard gelatin capsule over the same dose range. These results suggest differences in absorption with significantly greater blood glucose level drop at 48 mg daily dose of Glucosol™ in an oil-based soft gelatin formulation (Figure 2).

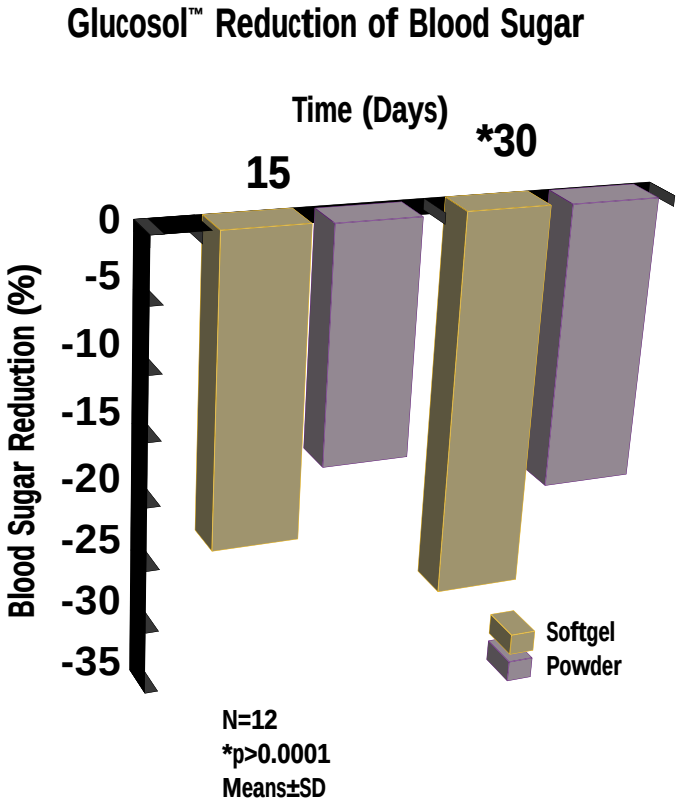

FIG2: Relative changes in blood sugars during softgel and powder Glucosol™ supplementation. Both Glucosol™ forms significantly reduced blood sugars. Changes with the softgel form were significantly ($p>0.001$) greater than those for the powder form at 15 and 30 days.

Measurement

The subjects were monitored for the following parameters: Blood glucose, blood pressure, body weight, temperature, heart rate, and general health and comfort in response to the supplement. Patient feed- back was also noted.

Cross-over Study

In the cross-over study design, a group of 12 subjects were given placebos for two weeks and their fasting blood glucose levels were monitored. The same group was given an oral daily dose of 48 mg Glucosol™ (two capsules of 8 mg Glucosol™ after each meal or a total of 6 capsules a day) in an oil-based soft gelatin formulation for 30 days. A (placebo) washout period of 45 days was allowed. After the initial washout period, the same group was crossed over to a daily 48 mg Glucosol™ treatment (two capsules of 8 mg Glucosol™ after each meal or a total of 6 capsules a day) in a dry-powder hard gelatin formulation for a period of 30 days. Following the hard gelatin Glucosol™ treatment, a second washout period of 45 days was allowed. The blood glucose levels were monitored at 15-day intervals, during the dosing and washout periods.

The Outcome

The results of this cross-over study demonstrate that an oral dose of Glucosol™ is effective in reducing blood glucose levels, with no signs of adverse effects. The average blood glucose level in the control group was 168.3 ± 10.3 mg/deciliter and the soft gelatin formulation caused a rapid drop to an average value of 127.2, and 115.1 mg/ deciliter at the 15th and the 30th

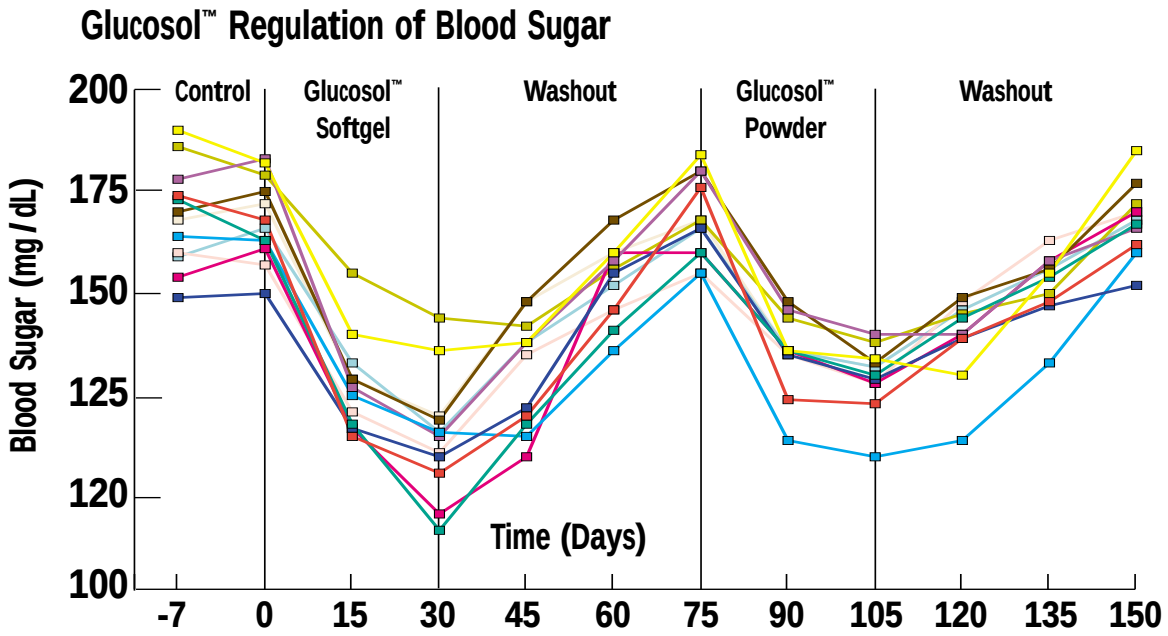

FIG3: Influence of Glucosol™ softgel and dry powder formulations on blood sugar regulation in Type II Diabetic patients. Glucosol™ was given at a dose of 48 mg/day (16 mg after each meal). Individual patient responses are present. Controls were from -7 to 0 days. Crossover was at 75 days. The active supplementation period was from 0 to 30 days (softgel) and 75 to 105 days (dry powder). The first washout period was from 30 to 75 days, and the second at 105 days. All volunteers responded to Glucosol™ supplementation with various rates and magnitudes of fasting blood sugar reduction. During the washout interval, the recovery of blood sugar was delayed in all volunteers for 45 days.

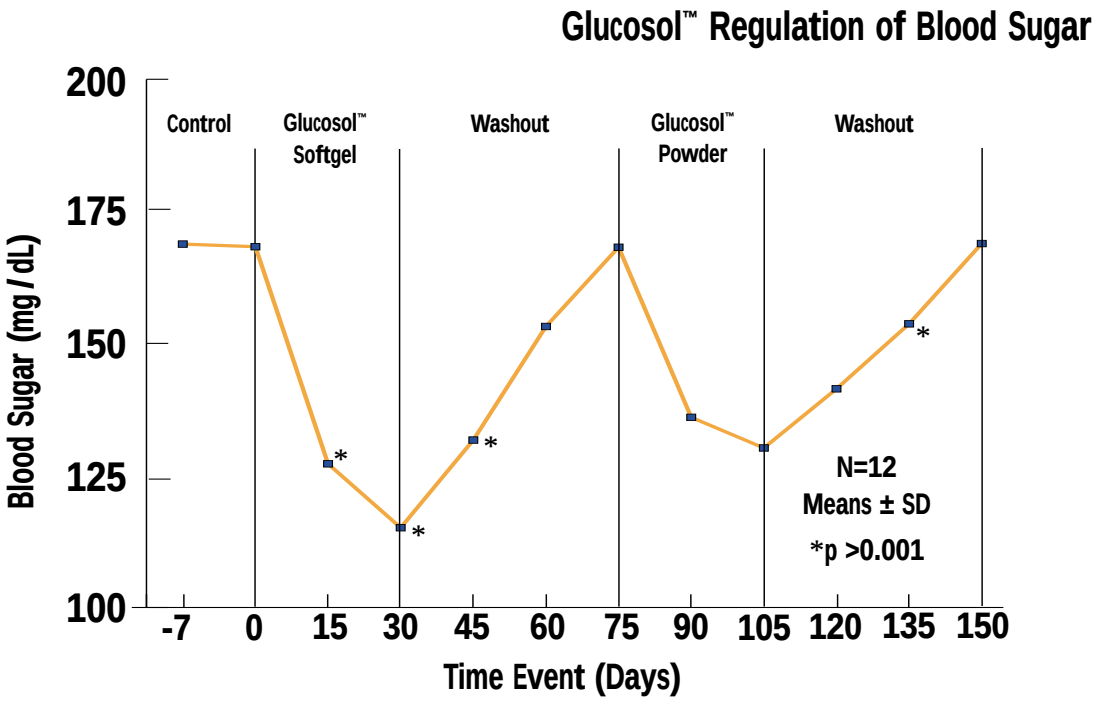

FIG4: Group mean blood sugar responses in a group of Type II diabetics (N=12) to 48 mg/day of a softgel and a dry powder Glucosol™ formulation. Note the rapid blood sugar reduction in the initial 15 days of supplementation and a gradual change thereafter for both Glucosol™ formulations. Significant blood sugar reductions occurred for both formulations, however the 30 day group response was significantly ($p<0.001$) greater for the softgel Glucosol™ formulation.

day of Glucosol™ treatment, respectively. During the washout period, the recovery of the blood glucose level was slow (131.7, 153.2 and 168.2 mg/deciliter at 15, 30 and 45 day of washout period). The washout period blood glucose levels suggest a memory effect of Glucosol™ for up to four weeks, even after the termination of the treatment (Figure 3).

After the initial washout period, a cross-over to 48 mg daily Glucosol™ treatment in a dry-powder hard gelatin capsule formulation brings the blood glucose levels down but not to the same degree as the soft gelatin formulation. In the washout period, following the treatment of hard gelatin formulation of Glucosol™, the memory effect of Glucosol™ treatment is notable in the slow recovery of blood glucose levels (Figure 3).

Compared to the dry-powder formulation treatment, a significantly greater drop in the average blood glucose level is observed with the soft gelatin formulation of Glucosol™.

Furthermore, these results indicate that both formulations, at 48 mg Glucosol™ per day, show continued blood glucose reduction until the end of the 30-day period. However, the soft gelatin formulation demonstrates a comparatively rapid and significantly greater blood glucose level drop at both 15 and 30 day period compared to the hard gelatin formulation. Furthermore, the greatest decrease of blood glucose to Glucosol™ treatment seem to occur in the first 15 days in both formulations (Figure 4).

Regaining Blood Glucose Balance

Glucosol™ supplementation seems to help in regaining blood glucose balance in adult onset diabetes (Type II) compared to pre-treatment control. Steeper decline in blood glucose levels and maintenance of lower blood glucose levels are evident in Glucosol™ supplementation compared to control conditions (Figure 5).

Furthermore, Glucosol™ treatment shows sharper decline in blood glucose level after a meal resembling normoglycemic profile compared to the slow decline observed in (diabetic) untreated control condition (Figure 6). Subjects under Glucosol™ supplementation report disappearance of conditions associated with adult onset diabetes, such as frequent thirst and urination.

Glucosol™- Blood Sugar Levels

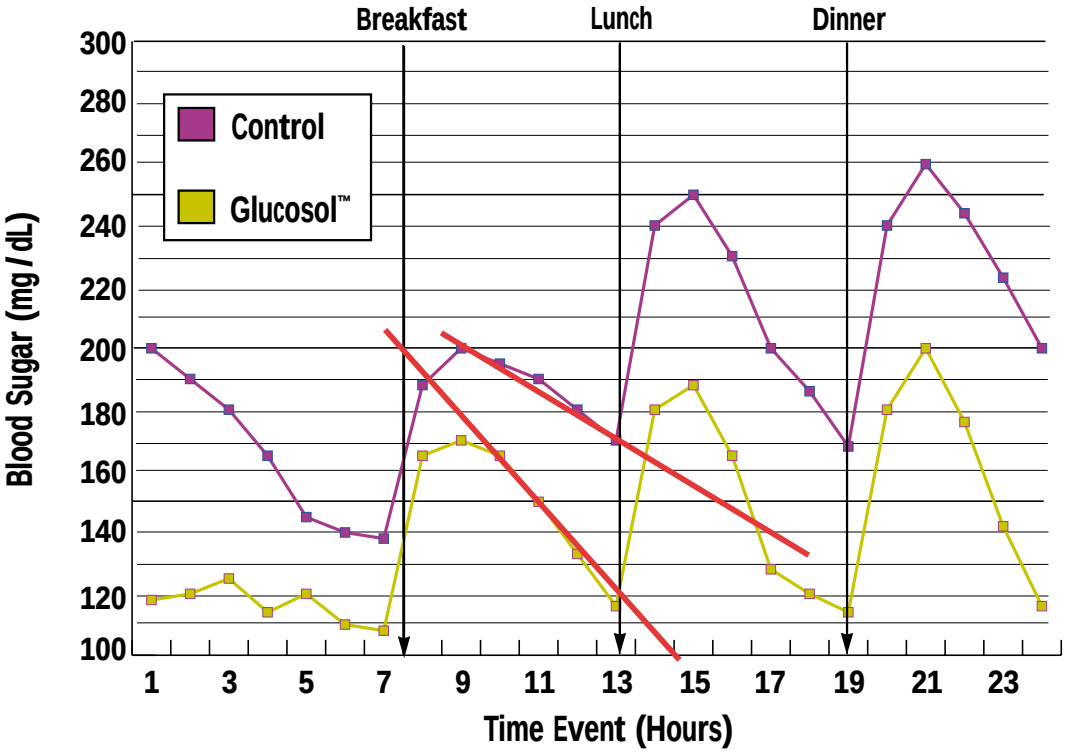

FIG5: Hourly blood sugar levels in Type II Diabetic patients before and after 30 days of 48 mg/day Glucosol™ supplementation. Note the apparent steeper decline and the lower minimal blood sugar level during Glucosol™ supplementation compared to the control study. These differences (20 vs 11 mg/dL/hour) between Glucosol™ and the control conditions shows that the rate of sugar transport during Glucosol™ supplementation is twice that for the control condition.

Blood Sugar Variations Before and During Glucosol™ Supplementation

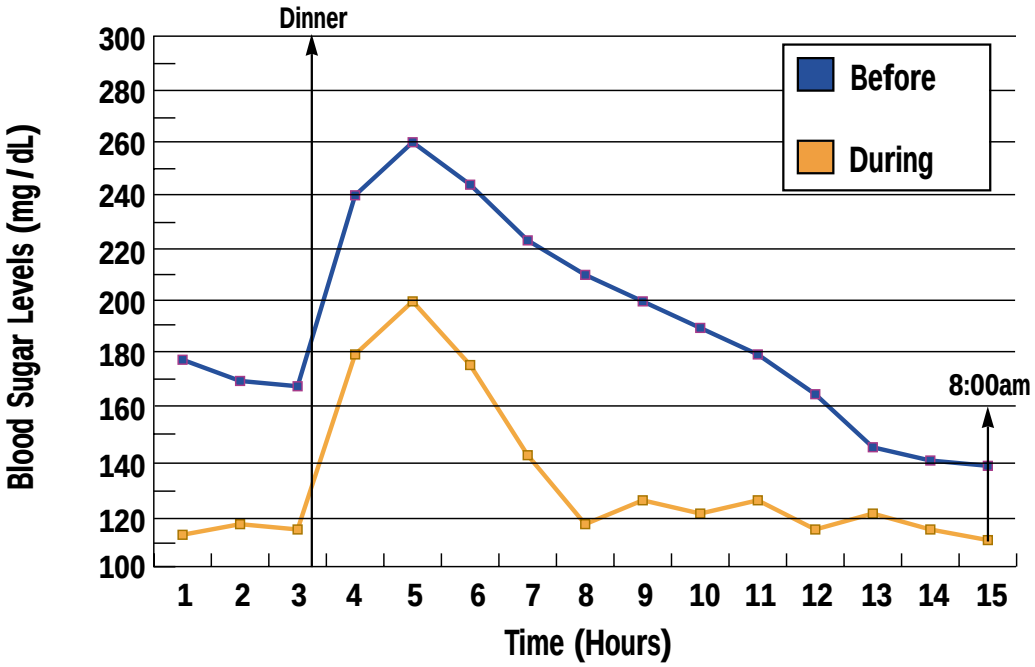

FIG6: Hourly blood sugar levels in a Type II diabetic patient before and during (30 days) Glucosol™ (48 mg/day) supplementation. Note the similar rise in blood sugar after the evening meal, but the slow decline in blood sugar before, compared to that during Glucosol™ supplementation. The fifteen hour data points are the fasting glucose levels. The blood sugar profile during Glucosol™ is more representative of that found in normal sugar regulation, whereas the slow sugar decrease after a meal is the characteristic of a Type II Diabetic.

Weight Loss

Subjects receiving the oil-based Glucosol™ formulation in a soft gelatin capsule seem to show an increased tendency of weight loss (an average weight loss of 3.2 pounds) than a dry-powder based Glucosol™ formulation (an average weight loss of 2.6 pounds) (Figure 7).

Mechanism of Action

Several types of glucose transporters are known in cell membranes of mammalian tissues. A glucose transporter is important in regulating the level of intracellular glucose. Glucose transport is one of the most important functions of all cells to acquire energy.

Glucosol™ and Body Weight Change

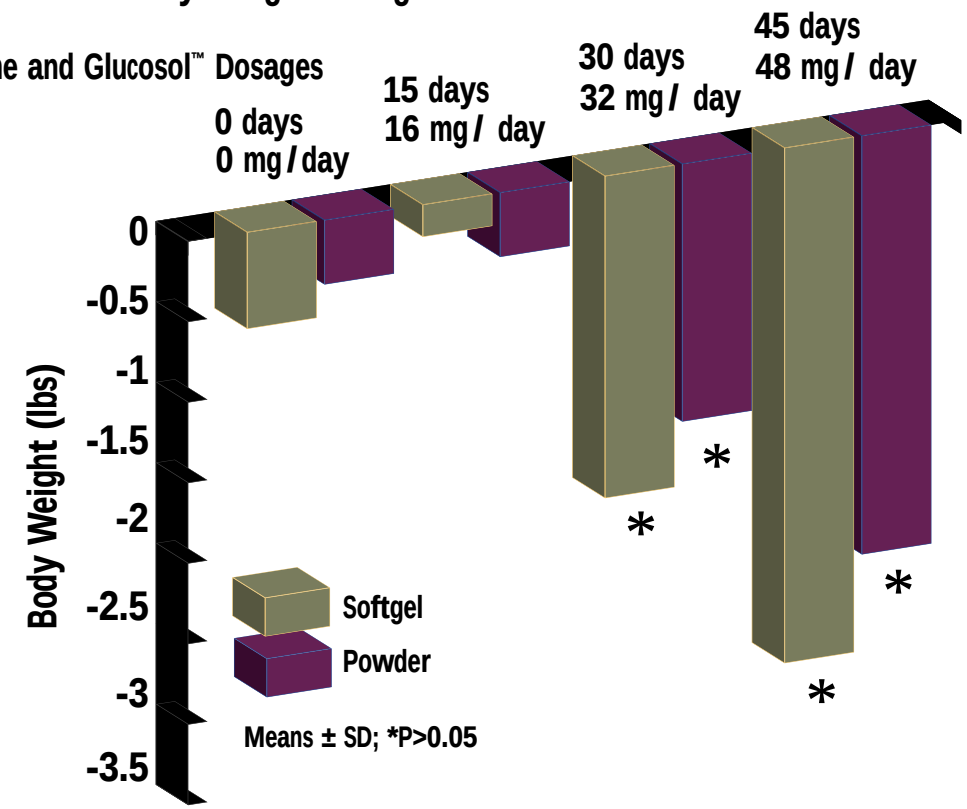

FIG7: Body weight change in Type II Diabetics during supplementation with 16, 32, and 48 mg/ day Glucosol™. Supplementation time for each dose was 15 days. Both the softgel and powder forms of Glucosol™ decreased body weight significantly at the 32 and 48 mg/day dosages. The difference between Glucosol™ forms was not statistically different.

Modifications of the activity of glucose-transport would cause several physiological effects, such as lowering glucose level. Only a few compounds have been known to affect glucose transport activity. For example, forskolin is a known glucose transport inhibitor and is useful as a control for *in vitro* test of glucose uptake. Therefore, finding an activator of glucose transport is more beneficial. Ehrlich ascites tumor cells are useful to measure glucose transport activity because these cells are known to contain a glucose transporter and they can be easily propagated and are thus useful as a simple experimental system for screening glucose transport activity of natural products and extracts.

The time course of 2-deoxy-D-glucose (2-DG) uptake by Ehrlich cells was measured and the rate of uptake was linear up to 2 minutes at concentrations of 0.2 to 1.0 mM. In this system, forskolin inhibited 2-DG uptake by 51%, at a concentration of 20 µM, and used as a control.

Corosolic acid, the active ingredient in Glucosol,™ showed a significant glucose transport-stimulating activity, at a concentration of 1 µM (Figure 8). A recent report indicates that oral administration of Corosolic acid in normoglycemic rats resulted in hypoglycemic effect and this result correlates with the above glucose uptake in vitro assay.

Glucosol™ is Different from Insulin

Glucose transporters are important in regulating the level of intracellular glucose and, as noted above, insulin increased this glucose transporter activity.

Insulin, however, is temperature sensitive while Glucosol™ is temperature insensitive. Oral administration of insulin does not produce hypoglycemic effect, or drop in blood sugar level, whereas Glucosol™ does show hypoglycemic effect. Large doses of insulin injected parenterally, produces convulsions or death, while oral dose of Glucosol™ does not have any side effects.

Hence, Glucosol™ is called phyto-insulin or insulin-like principle.

FIG8: Effect of Corosolic Acid on 2-DG Uptake (% of Control) by Ehrlich Cells

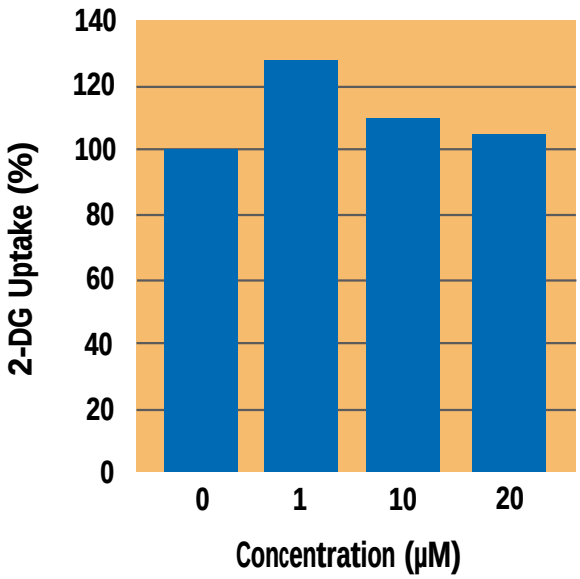

FIG8: Corosolic acid, the active ingredient in Glucosol,™ showed a significant glucose transport-stimulating activity, at a concentration of 1 μM.

Conclusion

Glucosol™ is a clinically proven potent natural product for formulations to activate cell glucose-transporter "shuttles" and thus help balance blood glucose levels. Glucosol™ shows a memory effect of blood glucose lowering even after the treatment is stopped. An oil-based Glucosol™ formulation in a soft gelatin capsule seems to be relatively more efficient in lowering blood glucose levels, perhaps through increased absorption.

These latest U.S. clinical study results confirm the 1998 Japanese clinical study results that Glucosol™ safely and effectively lowers blood glucose levels naturally in Type II diabetics.

Glucosol™ also delivers a strong anti-oxidant activity to scavenge free radicals and to prevent cell membrane lipid peroxidation. In addition, Glucosol™ helps maintain low blood pressure and normal kidney function.