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# A new Herbal preparation with hypoglycemic effect used in treatment of Non Insulin Dependent Diabetes Mellitus [NIDDM]

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**الخلاصة:**

تم تحضير خلطة عشبية عالية الجودة من مجموعة من الإعشاب الطبية وهي الأجزاء الهوائية لنبات الشيح (ربع جزء)، بذور الترمس (ربع جزء), بذورا لحلبة (ربع جزء), بذور الحبة السوداء (جزء واحد) لتكوين خليط مطحون ومتجانس موزع بصورة متساوية على كبسول جيلا تيني صلب من الحجم (صفر) يزن≈ 700 ± 10 ملغم للكبسولة الواحدة.

تم استعمال هذه الخلطة من قبل مجموعة مكونة من إحدى وأربعين حالة من مرضى السكري (النوع الثاني) وبجرعة كبسولة واحدة ثلاثة مرات يوميا بعد الطعام لمدة شهر واحد أما المجموعة الأخرى (إحدى وأربعين حالة من مرضى السكري, النوع الثاني) فكان علاجها بدواء المتفورمين (500 ملغم) ثلاث مرات يوميا بعد الطعام. تم قياس مستوى السكر في الدم بوضع الصائم وللمجموعتين قبل العلاج وبعد العلاج لمدة شهر على فترة فحص كل ثلاثة أيام بالأسبوع وبأخذ المعدل الشهري العام ومقارنة النتائج مع تحليلها إحصائيا قبل وبعد العلاج وجد انخفاض في تركيز السكر في الدم للمجموعتين وبشكل ملحوظ إحصائيا مع تحسن ملحوظ للمرضى الذين استخدموا العلاج العشبي مقارنة بالمجموعة الأخرى.

## Abstract:

Highly qualified herbal mixture prepared from; *Artemisia herba Alba* [aerial parts], *Lupinus albus* [fruits], *Trigonella foenum-graecum* [fruits], and *Nigella sativa* [fruits], in a proportion of [0.25 part: 0.25 part: 0.25 part: 1 part], mechanically milled to a uniform mesh size and homogenously fill size "0" hard gelatin capsules weight ≈ 700 ±10 mg .

Forty-one [NIDDM] patients use this mixture for one month in a dose of one capsule three times daily after food assigned Group B. Another Forty-one [NIDDM] patients assigned Group A, are using Metformin tablets 500 mg three times per day after food for one month. Pre- and post- treatment of fasting blood glucose levels of both Groups recorded on three days interval per week for one month, the monthly average counted and the results analyzed statistically to show significant lowering of blood glucose for both groups after treatment, with significant improvement of blood sugar by Herbal medicine compared to Metformin.

## Introduction:

Diabetes mellitus is a common chronic disease affecting millions of people worldwide. Standard treatment is failing to achieve required correction of blood glucose in many patients. Therefore, there is a need for investigating potential hypoglycemic drugs or herbs to improve glycemic control in diabetic patients [1]. The present number of diabetics worldwide is over 150 million and this is likely to increase to 300 million or more by the year 2025 [2]. Non-insulin-dependent diabetes mellitus or adult-onset diabetes is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency [3].

***Artemisia herba-alba* [white wormwood] Family: Asteraceae:**

The essential oil of *Artemisia herba-alba* exhibited anti-diabetic activity in alloxan-induced diabetic rats [4]. *Artemisia herba-alba* has an effect on heart rate and some hematological values in normal and alloxan induced diabetic rats [5]. Mohamed et al study the Chemical constituents and biological activities including hypoglycemic effect of *Artemisia herba-alba* [6]. *Artemisia herba-alba* Asso used in Moroccan folk medicine to treat arterial hypertension and/or diabetes [7, 8]. Present findings support the possible use of the essential oil of *Artemisia herba-alba* as a remedy for diabetes mellitus in humans [4]. Adult dose of *Artemisia herba-alba* is 3- 5 gm of dry herb per day [9].

***Lupinus albus* [termis] Family: Leguminosae:**

*Lupinus albus* or white lupin is considered a rich source of protein with a notable content of lysine and is being increasingly used in bakery, confectionery, snacks and pastry products due to its multifunctional properties, in addition to its potential hypocholesterolemic and hypoglycemic properties [10]. *Lupinus albus* is used in treatment of high fat diet induced type 2 diabetes in C57BL/6J mice [11]. An invention relates to the use of lupin conglutin gamma and of proteins showing homology higher than 50% with lupin conglutin gamma for the preparation of a medicament, food supplements or foods for the treatment of type II diabetes [12]. The hypoglycemic effect of lupin meal was described also recently by Mario Villaroel et al which suggest the use of plums jam containing lupin meal for use as dietetic food for diabetics [13] . The prevalent protein fraction in lupin seeds is the globulin one, which accounts for 87% of the total proteins, conglutin gamma accounts for about 6% of the total globulins [12]. Terruzzi, P. et al show the insulin-mimetic action of conglutin-γ, a lupin seed protein, in mouse myoblasts [14]. Dosage may vary, according to the symptoms, weight of the patient, severity of the disease in case of an adult human patient, the total daily dosage of lupin conglutin gamma will range from 150 to 750 mg, preferably from 50 to 250mg, in a single dose or in multiple doses, for example one to three times a day [12] .

***Trigonella foenum-graecum* [fenugreek] Family: Fabaceae:**

*Trigonella foenum-graecum* is one such plant that has been extensively used as a source of anti-diabetic compounds, from its seeds, leaves and extracts

in different model systems [15]. Preliminary human trials and animal experiments suggest possible hypoglycemic and anti-hyperlipedemic properties of fenugreek seed powder taken orally [16]. Broca et al. reported that 4-hydroxyisoleucine (4-OH-Ile), an amino acid extracted and purified from fenugreek seeds, displays an in vitro insulin tropic activity, which is of great interest, and that its stimulating effect is related to the immolation of glucose concentration in the medium as shown in isolated pancreatic beta cells [17] . 4-Hydroxyisoleucine is only found in plants, and owing to its particular insulin tropic action [17], it might be considered as a novel secretagogue with potential interest for the treatment of type II diabetes, a disease characterized by defective insulin secretion associated with various degrees of insulin resistance [18].

Administration of *Trigonella foenum- graecum*, seed powder to diabetic animals has been shown to lower blood glucose levels and partially restore the activities of key enzymes of carbohydrates and lipid metabolism to near normal levels in various animal models [19]. Water extract of *T. graecum* exhibited highest hypoglycemic and antihyperglycaemic activity (most active) in rats among all the extracts and may use as complementary medicine to treat the diabetic population by significantly reducing dose of standard drugs [20]. The components responsible and the mechanism by which Trigonella exerts their effects are not clearly understood; however earlier studies have shown the presence of steroid saponins in Trigonella seeds [21]. Saponin compounds diosgenin, alkaloids and trigonelline inhibit intestinal glucose uptake in vitro [22]. Extensive reviews have been written of health benefits on physiological effects of *Trigonella foenum-graecum* (fenugreek) and therapeutic applications in animal system as well as on humans, including anti diabetic and related physiological phenomenon [15, 23]. Basch et al. had reviewed the literature on the safety and adverse effects of *T. foenum-graecum* [21] although fenugreek has traditionally been considered safe and well tolerated; some side effects have been associated with its use [24]. Other reported side effects include transient diarrhea and flatulence [25]. Toxicological evaluation of diabetic patients taking fenugreek seed powder at a dose of 25 gm per day for 24 weeks showed no clinical hepatic or renal toxicity and no hematological abnormalities [26] .

***Nigella sativa* [black cumin] Family: Ranunculaceae:**

Nigella sativa has been reported to induce reduction in plasma glucose levels in alloxan-induced diabetic rabbits [27], as well as in streptozotocin induced diabetic rats [28-30], and found to be very effective in restoring glucose homeostasis in sand rat models [31]. *N. sativa* extract may prove clinically useful in the treatment of diabetics and in the protection of β-cells against oxidative stress in streptozotocin-induced diabetic rats [32]. *Nigella sativa* seeds were used as an adjuvant therapy in patients with diabetes mellitus type 2 added to their anti-diabetic medications in a dose of 2 gm/day [1]. Previous studies did not reveal any harmful effect of *Nigella sativa* on renal and hepatic functions on the contrary; the reported pharmacological actions of *Nigella sativa* oil include

protection against nephrotoxicity and hepatotoxicity induced by diseases, drugs or chemical compounds [33-37]. The antioxidant and anti-inflammatory activities of *Nigella sativa* are considered the main factors responsible for its nephroprotective and hepatoprotective effects [38]. *N. sativa* safely given to human patients in some clinical trials [39]. A dose of 1.5 gm powder of *Nigella sativa* (in two capsules) was given twice a day for one month, reduction in fasting blood sugar was not significant probably due to smaller dose of Nigella sativa used in this trial no side effects were detected in the treatment group [40].

## Materials and Methods:

### Preparation of Herbal medicine

Highly qualified, pure, and authenticated plant parts are collected from the local market of herbs in Baghdad, *Artemisia herba Alba* [aerial parts], *Lupinus albus* [fruits], *Trigonella foenum-graecum* [fruits], and *Nigella sativa* [fruits]. Those parts are mixed and mechanically milled to a uniform mesh size mixture in a proportion of 250 gm: 250 gm: 250 gm: and 1 kg respectively, the last mixture is distributed to make a homogenously filled size "0" hard gelatin capsules weigh ≈ 700 ±10 mg using capsule-filling machine: Capsuline®-15.

### Preparation of the study Groups:

The present study conducted on newly detected patients of [NIDDM], after final diagnosis and considering inclusion and exclusion criteria patients enrolled in this prospective study. The participants informed of all possible expected benefits and possible harm that may result from the study and written consent obtained from the study subjects.

### Inclusion criteria:

**1.** Abdominal obesity: Waist circumference
>102 cms for males
>88 cms for females
Waist circumference, measurement technique

To measure waist circumference, locate the upper hip, bone and the top of the right iliac crest. Place a measuring tape in a horizontal plane around the abdomen at the level of the iliac crest. Before reading the tape measure, ensure that the tape is snug, but does not compress the skin, and is parallel to the floor. The measurement made at the end of a normal expiration [41].

**2.** Fasting blood sugar more than 110 mg % [42].

### Exclusion Criteria:

**1.** Pregnancy
**2.** Type I diabetes mellitus [IDDM]
**3.** Impaired liver function test
**4.** Patients of chronic renal disease

Eighty-two patients divided in to two Groups the 1st Group A which is use Metformin 500mg (Glucophage®) three times per day after food for one month

and the 2nd one is Group B, which is used one capsule of Herbal medicine three times per day after food for one month.

**Checking of blood glucose level:**

Fasting blood sugar levels in mg/dl checked, ten O'clock in the morning before taking the treatment and on three days interval per week for one month after taking the treatment, using Accu-Chek active, Roche Diagnostic GmbH, Germany.

**Statistical analysis:**

The entire statistics done by using Microsoft Excel (ME).

## Results:

The pre- and post-treatment results in mg/dl were tabulate with mean, standard deviation (SD) and standard error of mean (SEM) for each set as shown in table-1. Analysis of pre-treatment (base line) blood sugar value of both groups by (ME) using un-paired t-test [43] shows $p>0.01$ prove that both groups are diabetic patients.

Pre- and post treatment blood sugar levels of both groups are analyzed statistically using paired t-test shows $*p<0.01$, indicate a significant reduction of blood sugar after treatment as shown in table-2.

Un-Paired t-test of after- treatment blood sugar of patients of both groups, has show $*p<0.01$ indicating a better correction of the hyperglycemic blood levels by Herbal medicine compared to Metformin. The Blood sugar profiles of Groups A & B are represented by a chart developed from (ME) as Figure-1 and 2 respectively.

## Discussion:

The components of the herbal preparation under investigation have used to control diabetes mellitus in human. Our mixture designed to yield a competitive hypoglycemic formula in a quantity of each component not exceeding the allowed daily dose stated by official references. Since the adult dose of *Artemisia herba-alba* is 3- 5 gm of dry herb per day [9], Lupin conglutin gamma from *Lupinus albus* 150 to 750 mg, in a single dose or in multiple doses, for example one to three times a day [12], Fenugreek seed powder at a dose of 25 gm per day shows no toxic effects [26] and *Nigella sativa* seeds were used as an adjuvant therapy in patients with diabetes mellitus type 2 added to their anti-diabetic medications in a dose of 2 gm/day [1], the prepared herbal dosages form, deliver only ≈300:300:300:1200 mg of the previous herbs respectively per day. The hypoglycemic control offered by the herbal preparation under investigation is statistically significant compared to metformin and it is presented by the difference in percentage of base line glucose levels reduction as shown in figure-3. This may be due to synergistic effect of the active ingredients found in those herbs, which may need further studies to adjust the dose and duration of treatment accordingly.

| Group A | | Group B | |
|---|---|---|---|
| Baseline | After treatment | Baseline | After treatment |
| 320 | 175 | 400 | 140 |
| 315 | 160 | 330 | 140 |
| 310 | 145 | 320 | 150 |
| 220 | 135 | 315 | 135 |
| 220 | 125 | 270 | 145 |
| 215 | 125 | 230 | 105 |
| 215 | 165 | 220 | 110 |
| 210 | 160 | 215 | 105 |
| 210 | 155 | 210 | 115 |
| 210 | 150 | 210 | 115 |
| 205 | 135 | 210 | 120 |
| 200 | 120 | 195 | 125 |
| 200 | 130 | 195 | 110 |
| 187 | 120 | 190 | 115 |
| 186 | 120 | 190 | 110 |
| 185 | 114 | 183 | 95 |
| 185 | 120 | 180 | 115 |
| 180 | 110 | 180 | 105 |
| 180 | 115 | 180 | 110 |
| 180 | 110 | 175 | 120 |
| 180 | 114 | 174 | 85 |
| 170 | 95 | 170 | 115 |
| 170 | 95 | 170 | 110 |
| 170 | 115 | 170 | 95 |
| 170 | 113 | 166 | 115 |
| 166 | 110 | 165 | 120 |
| 165 | 85 | 165 | 115 |
| 160 | 130 | 165 | 105 |
| 160 | 115 | 160 | 80 |
| 160 | 115 | 160 | 70 |
| 160 | 95 | 160 | 95 |
| 160 | 117 | 155 | 105 |
| 160 | 105 | 155 | 80 |
| 160 | 95 | 150 | 85 |
| 155 | 80 | 150 | 95 |
| 150 | 115 | 150 | 115 |
| Group A | | Group B | |
| Baseline | After treatment | Baseline | After treatment |
| 150 | 130 | 145 | 95 |

| | | | | |
|---|---|---|---|---|
| | **145** | **115** | **145** | **80** |
| | **145** | **105** | **145** | **70** |
| | **140** | **90** | **140** | **85** |
| | **140** | **85** | **140** | **100** |
| **Mean** | **187.05** | **119.71** | **192.63** | **107.32** |
| **SD** | **43.1** | **22.51** | **57.49** | **19.24** |
| **SEM** | **6.73** | **3.52** | **8.98** | **3** |

**Table-1: The pre- treatment sugar level and mean of post treatment level in mg/dl of Group A (using Metformin) and Group B (using Herbal medicine).**

SEM = standard error of mean.

Standard error of mean = Standard deviation/square root of (n)

n = number of samples.

| **Groups** | **Baseline** | **After treatment** |
|---|---|---|
| Group A (n=41) | 187.05 ± 6.73 | 119.71 ± 3.52 ***, a** |
| Group B (n=41) | 192.63 ± 8.98 | 107.32 ± 3.00 ***, b** |

**Table-2: Analysis of Pre- and post treatment blood sugar levels of both groups by (ME) using paired t-test**

Data are expressed as mean ± SEM.

n= number of patients.

*P< 0.01 with respect to baseline value.

Non-identical superscripts (a, b) represent significant difference, P<0.01.

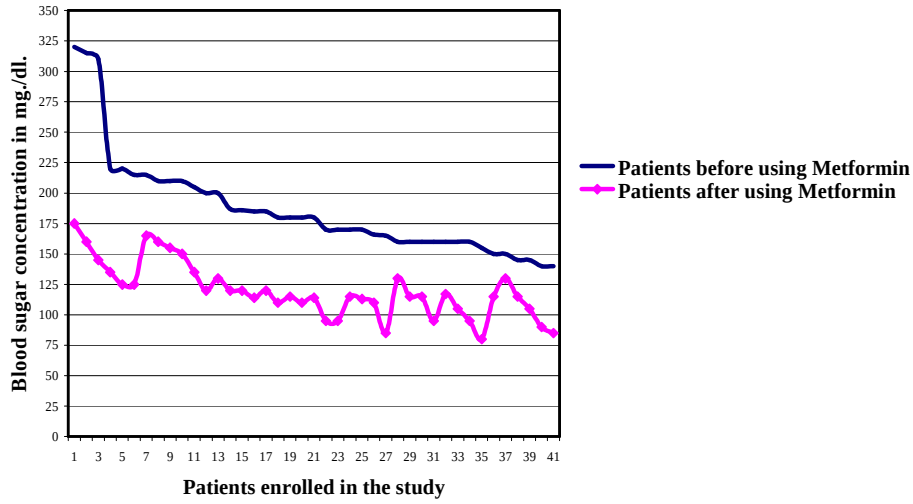


**Figure (1):** Blood sugar profile of group A

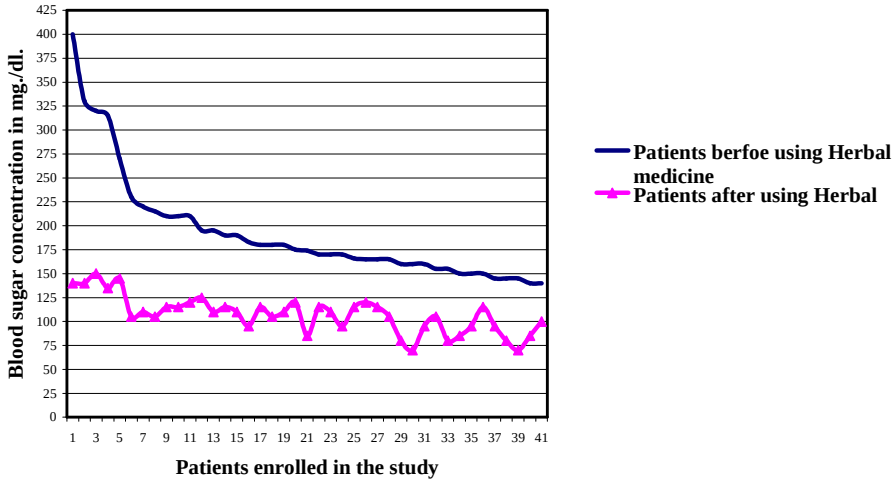


**Figure (2):** Blood sugar profile of group B

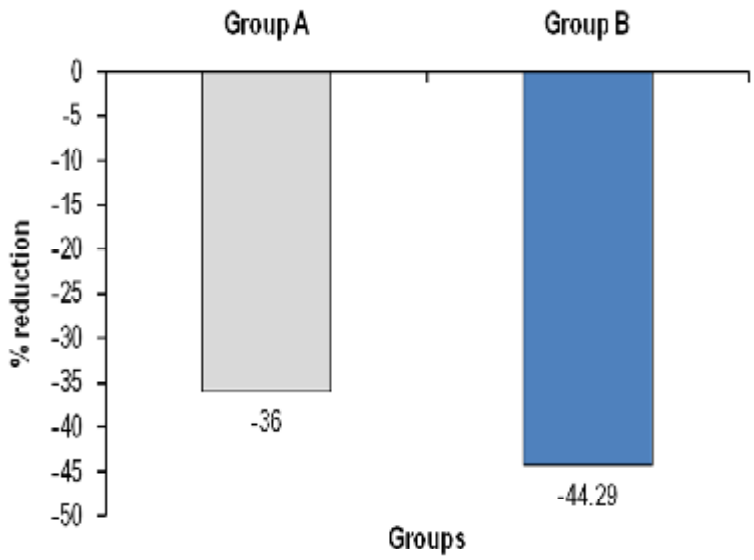


**Figure-3: percent of reduction in blood glucose level for patients using Metformin (Group A) and patients using the Herbal preparation (Group B).**

Percentage of reduction is calculated as follow

Percentage of reduction for each group = [(mean of glucose concentration after treatment multiplied by 100)/ mean of glucose concentration before treatment] minus 100…...equation no. 1

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