ESULIX®

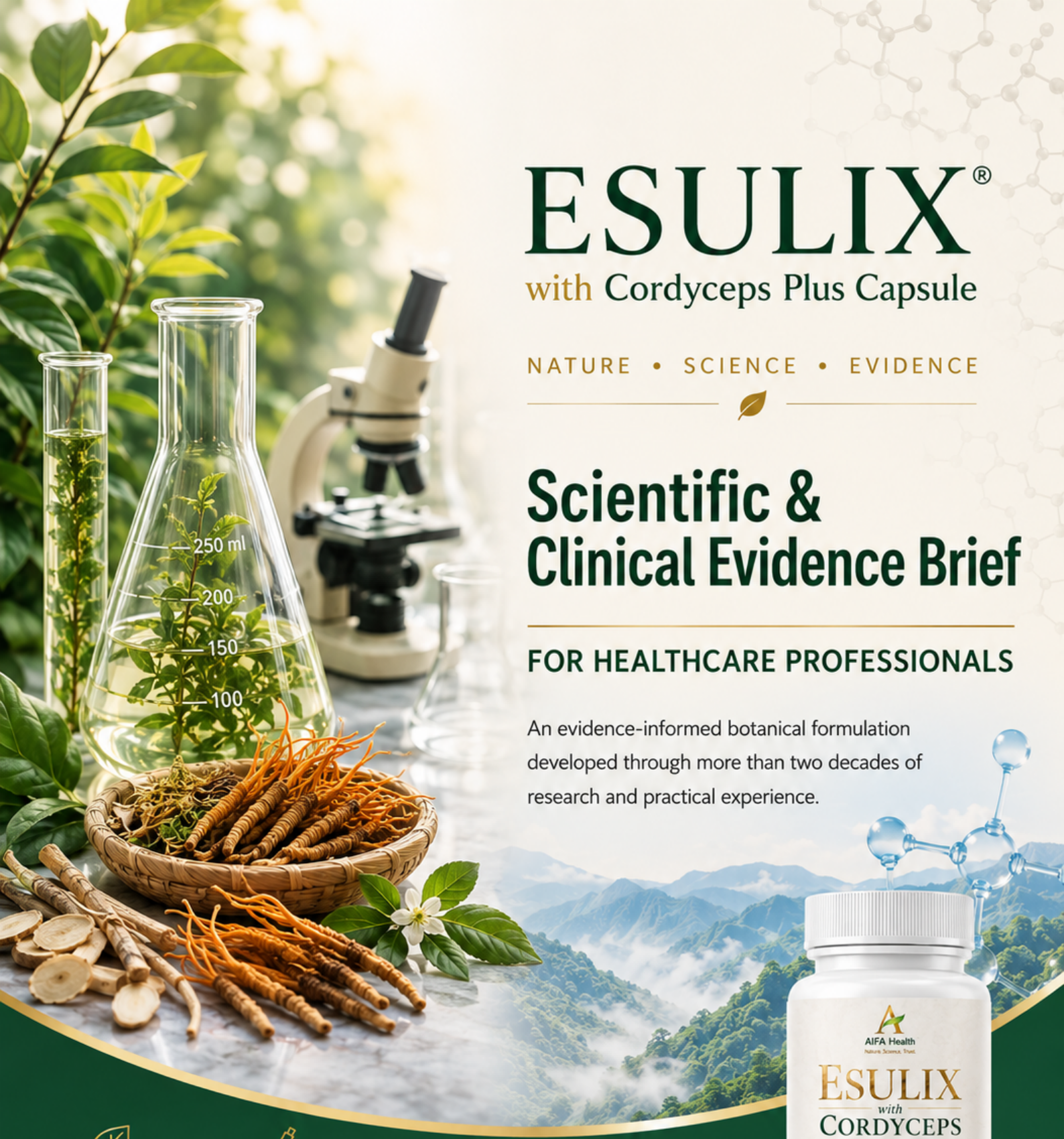
with Cordyceps Plus Capsule

NATURE • SCIENCE • EVIDENCE

Scientific & Clinical Evidence Brief

FOR HEALTHCARE PROFESSIONALS

An evidence-informed botanical formulation developed through more than two decades of research and practical experience.



BOTANICAL
Wisdom from traditional herbal heritage

SCIENTIFIC
Research-driven formulation and evaluation

EVIDENCE
Preclinical and preliminary human investigations

RESPONSIBLE
Transparent information for professional decision-making

Prepared for **healthcare professionals** committed to evidence-based, patient-centred diabetes care and holistic metabolic health.

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A Botanical Formulation with a Research History Spanning Nearly Two Decades

ESULIX® is a multi-botanical formulation developed from a combination of traditionally used botanical ingredients.

Its historical research journey has included preliminary human investigation, acute toxicity assessment, laboratory analysis, preclinical studies and later academic research.

RESEARCH JOURNEY

1. **2006–2007** — Early Clinical Study
2. **2009–2010** — Safety & Preclinical Research
3. **2013–2016** — USM Research Programme
4. **2015** — Historical GC-MS Screening
5. **2026 →** — The Esulix Chapter

EVIDENCE CONTEXT

The ESULIX® research history includes different forms of scientific investigation, each providing a different level of evidence.

Human evidence
Preliminary observations in people

Preclinical evidence
Experimental investigation of biological effects

Laboratory evidence
Characterisation and biological activity

Safety evidence
Assessment under specific experimental conditions

These different levels of evidence are complementary, **but they are not interchangeable.**

SCIENTIFIC AND CLINICAL EVIDENCE MAP

A MULTI-LAYERED EVIDENCE APPROACH FOR ESULIX®

The ESULIX® research history includes different forms of scientific investigation.

Each provides a different level of evidence and together they build a more complete understanding.

01 PRELIMINARY HUMAN EVIDENCE

Preliminary observations in people to explore the potential impact on metabolic markers and overall well-being.

EXAMPLE
Early clinical study in 20 patients (2006–2007)

02 SAFETY EVIDENCE

Assessment of safety under specific experimental conditions.

EXAMPLE
Acute toxicity study in animals (2009–2010)

03 LABORATORY & ACADEMIC EVIDENCE

Laboratory analysis, preclinical studies and university research to evaluate biological activities and potential mechanisms.

EXAMPLE
USM research programme (2013–2016) & MSc thesis (2016)

04 MECHANISTIC EVIDENCE

Investigation of biological mechanisms in vitro and in vivo to understand how the formulation may exert its effects.

EXAMPLE
Preclinical studies of a related historical formulation in animal models*

* The historical source refers to the investigated formulation as "Yimin". These findings provide supportive mechanistic context and are not direct evidence of effects from the current ESULIX® finished product.

EVIDENCE INTERPRETATION

The ESULIX® research history includes different forms of scientific investigation, each providing a different level of evidence.

These different levels of evidence are complementary, but they are **not interchangeable.**

IMPORTANT NOTE

ESULIX® is a health supplement. It is not intended to diagnose, treat, cure or prevent any disease. It should be used as part of a healthy lifestyle, including balanced diet, regular physical activity, and medical supervision when needed.

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PRELIMINARY HUMAN STUDY
(EARLY CLINICAL EVIDENCE)

A self-controlled clinical study to observe the effect of ESULIX® in patients with Type 2 Diabetes Mellitus and metabolic syndrome.

Study period
Jan 2006 – Jan 2007

STUDY DESIGN
Self-controlled (auto control) intervention study

PARTICIPANTS
22 recruited
2 discontinued
20 completed
(11 male, 9 female)
Age: 35–75 years (mean 55.8 years)

DURATION
12 weeks ESULIX® intervention with follow-up at 4, 8 & 12 weeks

CONCOMITANT TREATMENT
Conventional glucose-lowering medication continued.
Lipid-lowering drugs were discontinued.

MEASUREMENTS
See table below. Assessed at baseline and at 4, 8, and 12 weeks as applicable.

KEY RESULTS: BEFORE vs AFTER 12 WEEKS

(Mean ± SD, N = 20)

Parameter	Before Treatment (Baseline)	After 12 Weeks of ESULIX®	Change (After – Before)
Fasting Blood Glucose (FBG), mmol/L	8.05 ± 0.76	6.34 ± 0.64	↓ – 1.71
Postprandial 2 Hours Blood Glucose (P2hBG), mmol/L	10.89 ± 1.71	8.34 ± 1.54	↓ – 2.55
Fasting Insulin (FINS), µU/mL	29.05 ± 10.87	18.63 ± 5.89	↓ – 10.42
HOMA-IR* (reported as HCMA-IR in source)	14.38 ± 4.07	7.63 ± 2.67	↓ – 6.75
IAI* (1 / (FPG × FINS))	0.54 ± 0.34	0.75 ± 0.38	↑ + 0.21
Body Mass Index (BMI), kg/m²	28.96 ± 5.07	25.08 ± 4.67	↓ – 3.88
Glycosylated Hemoglobin (HbA1c), %	10.5 ± 3.2	7.15 ± 2.31	↓ – 3.35
C-peptide (Fasting), ng/mL	6.01 ± 1.72	4.05 ± 1.84	↓ – 1.96
Triglyceride (TG), mmol/L	2.58 ± 1.45	1.85 ± 0.94	↓ – 0.73
HDL-Cholesterol (HDL-C), mmol/L	0.64 ± 0.32	0.87 ± 0.48	↑ + 0.23
Fibrinogen, g/L	6.02 ± 0.84	4.26 ± 0.67	↓ – 1.76

Comparison before vs after treatment: $P < 0.01 – 0.05$ (as reported in the original study).
Note: Individual p-values for each parameter were not provided in the source.

INTERPRETATION

These are observed before-and-after findings from a small historical self-controlled study.
The study had no parallel placebo/control group, and conventional glucose-lowering treatment was continued.
The findings therefore warrant further controlled investigation and should not be interpreted as establishing that ESULIX® alone caused the observed changes.

WHAT THIS STUDY SUGGESTS

- ✓ Improvement in glucose control (FBG, P2hBG, HbA1c)
- ✓ Improvement in insulin sensitivity (FINS, HOMA-IR, IAI)
- ✓ Improvement in weight and lipid profile
- ✓ Improvement in fibrinogen level

Reference: Summary Report on Experimental Investigations of a New Drug in Malaysia "Esulin" – a new drug to treat Insulin Resistant. Jan 2006 – Jan 2007.

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PRECLINICAL / MECHANISTIC EVIDENCE

(IN VIVO ANIMAL STUDY – DIABETIC RATS)

Historical study of Yimin formulation (related to ESULIX® historical formulation) in a rat model of type 2 diabetes with insulin resistance

- This study investigated the effects and mechanisms of Yimin formulation on hyperglycemia and insulin resistance in diabetic rats.
- Metformin was used as a comparator.

SOURCE

Wang SR, Wang ZG
Journal of Chinese Medicinal Materials
2009;32(6):862–866

1 EXPERIMENTAL DESIGN

ANIMAL MODEL

Male SD rats (120–140 g)

Housing: 23 ± 2 °C, 12 h light/dark cycle, free access to food and water.

DIABETES MODEL

High-fat, high-sugar diet for 8 weeks + low-dose STZ 30 mg/kg (i.p.) to induce insulin resistance and hyperglycemia.

PHASE I* SCREENING

Multiple formulations/components and three doses of Yimin (low, middle, high) were tested for 8 weeks.

Middle-dose Yimin was selected for Phase II.

PHASE II* MECHANISTIC STUDY

Selected Yimin middle-dose formulation was evaluated for 8 weeks for mechanistic endpoints and compared with Metformin.

OUTCOMES ASSESSED

- Blood glucose, insulin, insulin sensitivity (ISI), glycosylated serum protein, glucagon
- Insulin receptors in liver-cell membrane (R1, R2)
- Skeletal muscle GLUT4 mRNA expression
- Pancreatic histopathology (β-cell number)

** Total duration of treatment in both phases: 8 weeks.*
STZ: Streptozotocin; GLUT4: Glucose transporter type 4;
ISI: Insulin Sensitivity Index = ln [1 / (Fasting Insulin × Fasting Blood Glucose)].

2 KEY MECHANISTIC FINDINGS (After 8 Weeks of Treatment)

A. INSULIN RECEPTORS IN LIVER-CELL MEMBRANE (R1, R2)

Compared with the diabetic model group, both Yimin (selected middle-dose) and Metformin groups showed significantly higher quantities of hepatic insulin receptors (R1 high-affinity and R2 low-affinity).

There was no significant difference between Yimin and Metformin groups ($P > 0.05$).

Affinity constants (R1/R2 ratio) did not differ significantly among groups.

- ✓ Model group had lower liver-cell insulin receptor quantities than normal control ($P < 0.01$).
- ✓ Yimin selected middle-dose and Metformin increased receptor quantities vs model group (* $P < 0.01$; ** $P < 0.05$).
- ✓ Between Yimin and Metformin: no significant difference ($P > 0.05$).

B. SKELETAL MUSCLE GLUT4 mRNA EXPRESSION (AVERAGE OPTICAL DENSITY)

Parameter	Normal Control (n = 10)	Model (Diabetic Control) (n = 10)	Metformin 200 mg/kg (n = 10)	Yimin (Selected Middle-Dose Formulation) (n = 10)	Significance vs Model Group
GLUT4 (AOD)	0.57 ± 0.04	0.27 ± 0.02 ##	0.49 ± 0.05 *	0.46 ± 0.04 *	* $P < 0.01$

$P < 0.01$ vs Normal Control
** $P < 0.01$ vs Model (Diabetic Control) group*

C. PANCREATIC β-CELL NUMBER (ROUTINE H&E STAIN, 400×; CELLS PER ISLET FIELD)

Parameter	Normal Control (n = 20 fields)	Model (Diabetic Control) (n = 18 fields)	Metformin 200 mg/kg (n = 19 fields)	Yimin (Selected Middle-Dose Formulation) (n = 18 fields)	Significance (as reported in Table 7 of the study)
β-Cell Number (cells/field)	58.20 ± 15.30	35.50 ± 13.51 *	42.17 ± 12.06 *, ▲	45.58 ± 15.06 *, ▲	* $P < 0.01$ vs Normal; ▲ $P < 0.01$ vs Model

** Compared with Normal Control was significant ($P < 0.01$)*
▲ Yimin (selected middle-dose) group vs Model group was significant ($P < 0.01$)
Statistics: Single-factor ANOVA (SPSS 13.0).

3 SUMMARY OF FINDINGS

Yimin (selected middle-dose formulation) increased hepatic insulin receptor (R1 & R2) quantities compared with diabetic model; comparable to Metformin.

Yimin significantly increased skeletal muscle GLUT4 mRNA expression compared with diabetic model.

Yimin significantly increased pancreatic β-cell number compared with diabetic model.

INTERPRETATION

In diabetic rats, Yimin formulation improved insulin receptor levels, skeletal muscle GLUT4 expression and pancreatic β-cell number, supporting improved insulin sensitivity and glucose homeostasis. These mechanistic findings provide

IMPORTANT NOTE

Yimin was the formulation investigated in this historical animal study. These findings are preclinical and not direct evidence for the current ESULIX® finished product. Metformin was an experimental comparator;

Source: Wang SR, Wang ZG. Studies on diabetic rats and insulin resistance. Journal of Chinese Medicinal Materials. 2009;32(6):862–866.

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LABORATORY SCREENING RECORD

CORTICOSTEROID ADULTERATION SCREEN

GC–MS analysis of Esulin aqueous extract

Historical record: 19 May 2015 (PRN2015/173)

SOURCE

National Poison Centre,
Universiti Sains Malaysia (USM), Penang

Record No. : PRN2015/173
Date of record : 19 May 2015
Sample : Esulin aqueous extract
(as stated in the laboratory record)

PURPOSE OF SCREEN

To screen the Esulin aqueous extract for the presence of eight specified corticosteroids using GC–MS.

RESULTS: EIGHT CORTICOSTEROIDS SCREENED

No.	Corticosteroid (Analyte)	LOD* (µg/g)	Result in Esulin Aqueous Extract (as per record)
1	Dexamethasone	37.5	ND (Not Detected)
2	Betamethasone	50.0	ND (Not Detected)
3	Cortisone	37.5	ND (Not Detected)
4	Hydrocortisone	37.5	ND (Not Detected)
5	Prednisone	37.5	ND (Not Detected)
6	Prednisolone	37.5	ND (Not Detected)
7	Methylprednisolone	37.5	ND (Not Detected)
8	Triamcinolone	100.0	ND (Not Detected)

ND = Not Detected
* LOD = Limit of Detection for the method used.

KEY TAKEAWAY

In this historical GC–MS screening record (19 May 2015, PRN2015/173), none of the eight corticosteroids listed above were detected in the Esulin aqueous extract at or above the stated LOD.

IMPORTANT QUALIFIER

- This was a targeted screen for the eight corticosteroids specified above only.
- The result applies to the tested historical Esulin aqueous extract at the time of analysis.
- It does not establish the absence of every possible adulterant or certify that all production batches are free from prohibited substances.
- This laboratory record is part of the historical research file and should be interpreted in context with other evidence.

This laboratory record is cited as Appendix B in the USM Master's thesis (Farah 'Atiqah Binti Ab Rahman, September 2016).

ANALYTICAL METHODOLOGY (AS STATED IN RECORD)

Gas Chromatography–Mass Spectrometry (GC–MS)
Targeted analysis for specified corticosteroids.

RESPONSIBLE USE STATEMENT

ESULIX with Cordyceps Plus Capsule is a registered traditional product (MAL12085047TC). This laboratory screening record does not replace medical advice, diagnosis or prescribed treatment.

SOURCE CITATION

National Poison Centre, Universiti Sains Malaysia (USM), Penang.
GC–MS Screening Record No. PRN2015/173, 19 May 2015. Sample: Esulin aqueous extract.
(Full record cited in Appendix B of Farah 'Atiqah Binti Ab Rahman, MSc Thesis, USM, September 2016.)

ESULIX®
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USAGE & SAFETY / PROFESSIONAL GUIDANCE

Practical information for healthcare professionals

SAFE & RESPONSIBLE USE

ESULIX® with Cordyceps Plus Capsule is a **registered traditional product for adult use.**
Appropriate use and monitoring are important for safety.

ADULT USE ONLY

- For adults aged 18 years and above.
- Not recommended for children.

1 RECOMMENDED USE

USUAL HISTORICAL GUIDANCE

2 capsules twice daily
(before breakfast and before dinner)

This is the recommended schedule documented in the historical Medical Guideline.

ALTERNATIVE HIGHER REGIMEN (HISTORICAL)

2 capsules three times daily
(before breakfast, lunch and dinner)

A higher historical regimen of 2 capsules three times daily is also documented in the historical Medical Guideline. Individual tolerability should be considered.

IMPORTANT
Dosage may be adjusted based on individual response and tolerability. Start with the usual guidance and review as needed.

2 SAFETY & TOLERABILITY

POTENTIAL GASTROINTESTINAL RESPONSES

Increased bowel frequency has been reported, particularly during the early period of use. Other possible reactions recorded historically include nausea, diarrhoea, abdominal pain, flatulence, weakness or sweating.

WHAT TO DO

- If troublesome gastrointestinal symptoms occur, consider reducing to 2 capsules twice daily.
- If symptoms persist, discontinue use and seek medical advice.
- Ensure adequate hydration.

DISCONTINUE AND SEEK MEDICAL ATTENTION
If signs of allergic reaction or any unusual or severe symptoms occur.

3 DRUG INTERACTIONS & MONITORING

WITH GLUCOSE-LOWERING MEDICATION

Historical studies reported changes in glycaemic parameters. When used concurrently with glucose-lowering medication, blood glucose monitoring is advisable.

- Monitor blood glucose more frequently.
- **Do NOT** automatically reduce or discontinue prescribed medication.
- Adjust prescribed therapy only under the direction of the treating healthcare professional.
- Advise patients to **recognise symptoms** of hypoglycaemia and seek appropriate medical advice.

4 PRECAUTIONS

Pregnancy
Should not be taken by pregnant women.

Breastfeeding
Should not be taken by breastfeeding mothers.

Medical Conditions
Use with caution in individuals with chronic illnesses. Seek medical advice.

Surgery
Patients scheduled for surgery should inform their treating healthcare team about all traditional products and supplements being used.

Monitoring
Regular monitoring of blood glucose and overall health is recommended.

5 STORAGE & HANDLING

- Store according to current product-label instructions.
- Protect from direct sunlight and moisture.
- Keep out of reach of children.
- Check the expiry date before use.

6 PROFESSIONAL COMMUNICATION POINTS

- ESULIX® is a registered traditional product (MAL12085047TC), not a medicine.
- Evidence includes human observations, safety studies, preclinical research and laboratory screening.
- Current evidence does not establish clinical efficacy in people.
- Encourage healthy lifestyle: balanced diet, regular exercise and regular medical follow-up.
- Document patient counselling, product use and monitoring in clinical records.

PROFESSIONAL DISCLAIMER

ESULIX® with Cordyceps Plus Capsule is not intended to diagnose, treat, cure or prevent any disease.
The information provided is for educational purposes only and should not replace professional medical advice.
Please consult a qualified healthcare professional for personalised guidance.

Use responsibly.
Monitor appropriately.
Support overall well-being.

Source: Historical Medical Guideline (Esulin) and supporting records in the ESULIX evidence file.

REFERENCES & DOCUMENTARY SOURCES

All evidence cited in this brief is drawn from historical records and supporting documents in the ESULIX evidence file.

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PRIMARY REFERENCES

1. **Acute Toxicity Test (Animal Study) – 2009**
   Report on Esulin Acute Toxicity Test (Animal Study), 2009
   National Poison Centre,
   Universiti Sains Malaysia (USM), Penang.

2. **Clinical Studies in the Intervention of ESULIN – 2006–2007**
   Clinical intervention study in Type 2 Diabetes (Insulin Resistance).
   Esulin Research Group.
   (20 patients, 12-week study; historical record)

3. **USM Research Record – 2013–2016**
   Phytochemical and Antihyperglycaemic Studies of Cordyceps sinensis and Esulin.
   Master's Thesis by Farah 'Atiqah Binti Ab Rahman, Universiti Sains Malaysia (USM), September 2016.
   (Includes laboratory assays and STZ-induced diabetic rat studies)

4. **Corticosteroid Adulteration Screen – 19 May 2015**
   GC–MS Analysis of Esulin Aqueous Extract (PRN2015/173)
   National Poison Centre,
   Universiti Sains Malaysia (USM), Penang.
   (Eight specified corticosteroids: Not Detected)

5. **Historical Medical Guideline – Esulin**
   Esulin Medical Guideline (Internal Document).
   Includes dosage guidance, safety considerations and user monitoring recommendations.
   (Historical reference document)

6. **Company Historical Record – Since 2009**
   Esulin launched in 2009; subsequently renamed Esulix.
   (Company historical record)

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ESULIX® with Cordyceps Plus Capsule
MAL120850477C
(Registered Traditional Product)
Registration does not mean it is a substitute for medical diagnosis, treatment or prescribed medicine.

DOCUMENT VERIFICATION

To view the full supporting documents and verification pack, scan the QR code or visit our website.

www.aifahealth.com

EVIDENCE IN CONTEXT

- The evidence file contains historical human, animal, laboratory and safety records.
- Different studies investigated Esulin, Yimin/related formulations and historical samples; they should not automatically be treated as direct evidence for the current ESULIX® finished product.
- Findings are presented as reported in the source records, including study limitations.
- Further controlled research is warranted to investigate the observations reported historically.
- ESULIX® is a registered traditional product and should not replace prescribed treatment or professional medical care.

This brief is intended for healthcare professionals for educational and reference purposes only.

PROFESSIONAL DISCLAIMER

The information in this brief is compiled from historical and preliminary scientific and clinical records related to ESULIX® with Cordyceps Plus Capsule. It is intended for professional reference only and should not be used as a basis for product claims beyond the documented evidence. Please consult a qualified healthcare professional for personalized patient care