



بسم الله الرحمن الرحيم

∞∞∞∞

تم رفع هذه الرسالة بواسطة / سلوي محمود عقل

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد





Bee Honey as a Therapeutic Modality for Children with Functional Dyspepsia

Thesis

*Submitted for partial Fulfillment of the Master Degree
in Pediatrics*

By

Amna Ali Eid Sayed

M.B., B.Ch. (2014)

Faculty of Medicine- Minya University

Under Supervision of

Prof. Dr. Mamdouh Abdulmaksoud Abdulrhman

Professor of Pediatrics

Faculty of Medicine, Ain Shams University

Dr. Yosra Mohamed Mohsen Awad

Lecturer of Pediatrics

Faculty of Medicine, Ain Shams University

*Faculty of Medicine
Ain Shams University*

2022



يقول الله تبارك وتعالى:

(وَأَوْحَىٰ رَبُّكَ إِلَى النَّحْلِ أَنِ اتَّخِذِي مِنَ الْجِبَالِ
بُيُوتًا وَمِنَ الشَّجَرِ وَمِمَّا يَعْرِشُونَ * ثُمَّ كُلِي مِنْ كُلِّ
الثَّمَرَاتِ فَاسْلُكِي سُبُلَ رَبِّكِ ذُلُلًا يَخْرُجُ مِنْ بُطُونِهَا
شَرَابٌ مُّخْتَلِفٌ أَلْوَانُهُ فِيهِ شِفَاءٌ لِلنَّاسِ إِنَّ فِي ذَلِكَ
لَآيَةً لِّقَوْمٍ يَتَفَكَّرُونَ)

(سورة النحل آية 68 - 69)



Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**,
the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound
gratitude to **Prof. Dr. Mamdouh Abdulkaksoud
Abdulrhuman**, Professor of Pediatrics, Faculty of Medicine,
Ain Shams University for his keen guidance, kind supervision,
valuable advice and continuous encouragement, which made
possible the completion of this work.*

*I am also delighted to express my deepest gratitude and
thanks to **Dr. Yosra Mohamed Mohsen Awad**, Lecturer
of Pediatrics, Faculty of Medicine, Ain Shams University, for his
kind care, continuous supervision, valuable instructions,
constant help and great assistance throughout this work.*

Amna Ali

List of Contents

Title	Page No.
List of Abbreviations.....	i
List of Tables	iv
List of Figures	vii
Introduction	1
Aim of the Work.....	3
Review of Literature	
Functional Dyspepsia	4
Complementary and Alternative Medicine (CAM)	37
Apitherapy	54
Patients and Methods.....	67
Results	77
Discussion	97
Conclusion	103
Recommendations	105
Summary	107
References	109
Arabic Summary	—

List of Abbreviations

Abb.	Full term
AG.....	Anethum graveolens L.
AP-1	Activator protein 1
AP-FGIDs	Abdominal pain-related functional gastrointestinal disorders
CAM.....	Complementary and alternative medicine
CCK	Cholecystokinin
CCK-AR.....	Cholecystokinin A receptor
CDI	Clostridium difficile infection
CDQ	The Clinical Dyspepsia Questionnaire
CgA.....	Chromogranin A
CHM	Chinese herbal medicine
COMT	Catechol-o-methyltransferase
COVID-19.....	Coronavirus disease-19
COX-1	Cyclooxygenase 1
DHSI.....	Digestive Health Status Instrument
DSSI	Dyspepsia Symptom Severity Index
EC	Efficacy criteria
EPS	Epigastric pain syndrome
FAPDs	Functional abdominal pain disorders
FD	Functional dyspepsia
FDSD	Functional Dyspepsia Symptom Diary
FGIDs	Functional Gastrointestinal Disorders
FMiT	Fecal microbiota transplantation
FODMAP	Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
GA.....	Gastric accommodation
GDNF	Glial cell line-derived neurotrophic factor

List of Abbreviations Cont...

Abb.	Full term
GDNF	Glial cell-derived neurotropic factor
GDSS	Glasgow Dyspepsia Severity Index
GE	Gastric emptying
GI	Glycemic index
GIT	Gastrointestinal tract
GNB3-C825T	Guanine nucleotide binding protein β 3 subunit C825T
GN β 3	G-protein β polypeptide-3
GOS	Global Overall Symptom Scale
GSRS	Gastrointestinal Symptom Rating Scale
<i>H. pylori</i>	<i>Helicobacter pylori</i>
H2Ras	Histamine-2 receptor antagonists
IBS	Irritable bowel syndrome
IL-17	Interleukin 17
LDQ	Leeds Dyspepsia Questionnaire
LFD	Low FODMAP diet
LPDS	Leuven Postprandial Distress Scale
MGDS	Modified Glasgow Dyspepsia Severity
MGDSS	Modified Glasgow dyspepsia severity score
MIF	Migration inhibitory factor
NDI	Nepean Dyspepsia Index
NF- κ B	Nuclear factor kappa B
NGF	Nerve growth factor
nNOS	Neuronal nitric oxide synthase
NSAIDs	Nonsteroidal anti-inflammatory drugs
PADYQ	Porto Alegre Dyspeptic Symptoms Questionnaire

List of Abbreviations Cont...

Abb.	Full term
PAGI-SYM.....	Patient Assessment of Upper Gastrointestinal Symptom Severity Index
PDS.....	Postprandial distress syndrome
PENFS.....	Percutaneous electric nerve field stimulation
PII.....	Peak incremental index
PPIs	Proton pump inhibitors
PROM	Patient-reported outcome measures
PYY.....	Peptide YY
QOL	Quality of life
RANTES.....	Regulated upon activation, normal T cell expressed and secreted
RCTs	Randomized controlled trials
RNA	Ribonucleic acid
SERT	Serotonin transporter
SF-NDI	Short-form Nepean Dyspepsia Index
SLDQ.....	Spanish Language Dyspepsia Questionnaire
SODA.....	Severity of Dyspepsia Assessment
STW5	Iberogast
TA	Trachyspermum ammi L
TCA.....	Tricyclic antidepressants
TDA	Traditional dietary advice
TEA.....	Transcutaneous electrical acustimulation
TNF- α	Tumor necrosis factor α
TRPV1.....	Transient receptor potential cation subfamily V1
VAS.....	Visual Analogue Scale
ZM.....	Zataria multiflora Boiss

List of Tables

Table No.	Title	Page No.
Table (1):	Showing pathophysiological substrates in FD.....	20
Table (2):	Alarm features suggesting further diagnostic testing.....	24
Table (3):	Overview of available patient-reported outcome measures	25
Table (4):	Modified Glasgow dyspepsia severity score.....	27
Table (5):	Available medications for treatment of FD in children.....	30
Table (6):	Common food with low FODMAP content	40
Table (7):	Common food with high FODMAP content	41
Table (8):	Comparison between baseline sociodemographic characteristics in groups A and B.....	78
Table (9):	Comparison between groups A and B as regards to symptomatology	79
Table (10):	Percentage distribution of FD subtypes in groups A and B	80
Table (11):	Comparison between groups A and B as regards baseline scores and sub scores.....	81
Table (12):	Comparison between both groups as regarding to the outcome of treatment at 4 weeks	82
Table (13):	Comparison between groups A and B as regards percentage of improvement and the outcome at W4	82
Table (14):	Comparison between both groups as regards percentage of improvement and the outcome at W8.....	83

List of Tables Cont...

Table No.	Title	Page No.
Table (15):	Comparison between both groups as regards percentage of improvement and the outcome at W12	83
Table (16):	Comparison between group A patients as regards total score interpretations at baseline and weeks (1-12).....	86
Table (17):	Comparison between group B patients as regards total score interpretations at baseline and weeks (1-12).....	87
Table (18):	Comparison between baseline, W4, W8 and W12 as regards total mean score in group A.....	88
Table (19):	Comparison between baseline, W4, W8 and W12 as regards total mean score in group B.....	88
Table (20):	Comparison between groups A and B as regards W2 sub scores	89
Table (21):	Comparison between groups A and B as regards W4 sub scores	91
Table (22):	Comparison between groups A and B as regards W8 sub scores	93
Table (23):	Comparison between groups A and B as regards W12 sub scores	94
Table (24):	Comparison between groups A and B as regards total mean score and mean sub score at W2	95
Table (25):	Comparison between groups A and B as regards total mean score and mean sub score at W4	95

List of Tables Cont...

Table No.	Title	Page No.
Table (26):	Comparison between groups A and B as regards total mean score and mean sub score at W8.....	96
Table (27):	Comparison between groups A and B as regards total mean score and mean sub score at W12.....	96

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Schematic representation of the (GIT) sensing of meal-related stimuli, and effects on GIT functions, appetite and energy intake	8
Figure (2):	Model of functional dyspepsia as a disorder of brain–gut signalling	13
Figure (3):	Summary of genetic polymorphism study.....	17
Figure (4):	Possible mechanisms by which LFD leads to improvement in FD	19
Figure (5):	Algorithm for the diagnosis and treatment of FD in adults	28
Figure (6):	Therapeutic algorithm for functional dyspepsia in children.	29
Figure (7):	The mechanisms of FODMAP in symptom generation in children	43
Figure (8):	Proposed effects of herbal preparations on various FGIDs.	45
Figure (9):	The important therapeutic effects of honey.....	56
Figure (10):	Flowchart.....	68
Figure (11):	Comparison between group A and B as regards total cure rate (100% improvement) at 2, 4, 8 and 12 weeks	84
Figure (12):	MGDS score time course (full analysis set; total mean score and 95% confidence intervals; t test P-value for change from day 0 to week 12)	85
Figure (13):	Comparison between group A patients as regards total score interpretations at baseline and weeks (1-12).....	86
Figure (14):	Comparison between group B patients as regards total score interpretations at baseline and weeks (1-12).....	87

INTRODUCTION

Functional Gastrointestinal Disorders ‘(FGIDs)’ define variable combinations of chronic gastrointestinal symptoms that do not have an identified underlying pathophysiology. Without an objective marker, the classification of FGIDs depends on symptoms. FGIDs are common in school-aged Egyptian children/ adolescents; functional dyspepsia (FD) prevalence was 4.6% (*Ibrahim et al., 2020*).

According to the Rome IV criteria for FD in children, FD was characterized by the presence of one or more bothersome symptoms, including epigastric pain or burning, early satiety, and post-prandial bloating that further track into FD subtypes (post-prandial distress syndrome, epigastric pain syndrome) that may exist alone or overlap with one another, after appropriate evaluation the symptoms cannot be fully explained by another medical condition (*Hyams et al., 2016*).

The impaired quality of life of patients with FD implies the need for definitive establishment of the diagnosis, followed by symptom-oriented treatment for the duration of the symptomatic interval (*Madisch et al., 2018*).

The treatment options can be classified as non-pharmacological or pharmacological. The primary goal is to achieve complete remission of the symptoms; if this is not possible, then the abdominal pain and its exacerbated episodes should be minimized (*Brusaferr et al., 2018*).

Antipsychotics, tricyclic antidepressants, histamine-2 receptor antagonists (H2Ras), standard and low-dose proton pump inhibitors (PPIs), acotiamide and mosapride, were found to be effective for FD (*Ford et al., 2021; Browne et al., 2018*).

Complementary and alternative (CAM) therapies offer the potential to be considered in alternate and mainstream treatment of FD (*Chiarioni et al., 2018*).

Synthetic medicines have side effects which leaves researchers to pay more attention to herbal medicine. Honey has been used since ages for medicinal and traditional purposes, and was accepted as a new effective medicine to cure many diseases (*Zafar et al., 2020*).

Honey supplementation increased gastric emptying time in protein energy malnutrition patients, this delay in gastric emptying time might be primarily a compensatory phenomenon and it was augmented by the use of honey (*Shaaban et al., 2010*).

Honey as a natural agent has a gastroprotective potential. It provides mucosa healing mainly via its antioxidants, anti-inflammatory, and cellular protective mechanism (*Fazalda et al., 2018*).

In considerations of scarce knowledge in this field, health attributes of bee honey as a reliable therapy to improve the symptoms of FD in children, deserve seeking for.

In this study we aim to assess the effect of bee honey as an adjuvant therapy among children with FD dyspepsia.

AIM OF THE WORK

- **Primary Objective:**

Effect of bee honey on functional dyspepsia as an adjuvant therapy among dyspepsia suffering children assessed by Modified Glasgow Dyspepsia Severity (MGDS) Score in comparison to age and sex matched controls

- **Secondary Objective:**

Effect of bee honey on recurrence of symptoms one month after stopping medications assessed by MGDS Score