HEXBIO® As A Biotherapeutic Agent

B-CROBES MARKETING (M) SDN BHD
TOPICS:

- Hexbio®
- Hexbio® for Diarrhea
- Hexbio® for Constipation
- Hexbio® for Nutrient Absorption, Immunity & Recovery
- Dosage & Administration
- Stool Assessment & Digestive Health
- Granulated Microbial Cell Preparation
- Efficacy Established
- Scientifically Proven Safe For Consumption
- On-going Clinical Trials At Local & International Major Hospitals
- Palatable Orange Flavour
- No Reported Side Effect
- No Preservative Added
- HALAL For Muslims Consumption
- Registered With National Pharmaceutical Control Bureau
- Manufactured In Malaysia & GMP Compliance
HEXBIO® & Diarrhea
Diarrhea

Body reabsorbing water

Normal

Intestines

Stool

Diarrhea

Excess water in stool. Body cannot reabsorb
# Types of Diarrhea

<table>
<thead>
<tr>
<th>Type</th>
<th>Condition</th>
<th>Caused</th>
<th>Efficacy, HEXBIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretory Diarrhea</td>
<td>Increase secretion activity or inhibition of absorption.</td>
<td>1. Cholera toxin</td>
<td>N.A.</td>
</tr>
</tbody>
</table>
| Osmotic Diarrhea          | Too much of water is drawn into the bowel, maldigestion.                  | 1. Osmotic laxatives  
2. Malabsorption  
3. Lactose intolerance  | Selective                                                                 |
| Motility-Related Diarrhea | Rapid movement of food through the intestines (hypermotility).             | 1. Menstruation  
2. Hyperthyroidism                                                        | N.A.             |
| Inflammatory Diarrhea     | Damage to the mucosal lining, which leads to a passive loss of protein-rich fluids, and a decreased ability to absorb these lost fluids. | 1. Bacterial/ viral/ parasitic infection  
2. Inflammatory bowel disease  
3. Antibiotic treatment  
4. Colon cancer | Most                                                                      |
Treatment of Acute Gastroenteritis in Infants (6-12 months)

From the study, 65 young children aged 6-12 months, suffering from acute gastroenteritis were treated daily until diarrhea resolution. As showed in the result, the feeding of microbial cell preparation reduced the severity and duration of acute gastroenteritis in young children.

Raanan Shamir et. al, Evaluation of a diet containing probiotics for the treatment of mild diarrheal illness in children younger than one year of age, American College of Nutrition 2005; 24(Suppl. 5):370-375
61 children that tested positive for rotavirus were treated with microbial cell preparation/placebo for 6 days. Stools were collected and examined again after 6 days of treatment. In conclusion, oral administration of microbial cell preparation is effective in reducing the duration of rotavirus excretion.

Guarino A et. al, Oral bacterial therapy reduces the duration of symptoms and of viral excretion in children with mild diarrhea, Department of Pediatrics, University Federico II of Naples, Italy
Combined Treatment (with ORS) of acute diarrhea in children

37 children aged 3 to 24 months received ORS as a form of rehydration, and were treated to microbial cell preparation at 12-hours interval until the resolution of diarrhea.

In conclusion, addition of microbial cell preparation to ORS was effective in the treatment of children with acute diarrhea by decreasing the duration of diarrhea.

Simakachorn N. et. al, Clinical evaluation of the addition of lyophilized Lactobacillus LB to oral rehydration therapy in the treatment of acute diarrhea in children, Journal of Pediatric Gastroenterology and Nutrition 0277-2116
It is important to note that probiotic therapy of acute diarrhea should be combined with rehydration if available. Current WHO recommendations state that clinical management of acute diarrhea should include replacement of fluid and electrolytes losses along with nutritional support (WHO, 1995). Oral rehydration salts (ORS) have been widely used in such disease management, and it is within this context that the combination therapy with probiotics is hereby advocated. Effects such as probiotic restoration of the non-pathogen dominated intestinal microflora secondary to infection, maintaining mucosal integrity and improving electrolyte balance could have a significant impact on programs of treatment and prevention of acute diarrhea in developing countries.

Gilliland et. al. (2001). Health and nutritional properties of probiotics in foods including powder milk with live Lactic Acid Bacteria, WHO/FAO
The largest meta-analysis to evaluate 34 different clinical trials involving 4844 patients.

Result:
- Reduced the likelihood of developing antibiotic-associated diarrhea by 52%.

Conclusion:
- The benefits were most pronounced among children.

### Mode Of Action

**Hexbio**
- Suppressing the growth of pathogens through secretion of antimicrobial substances
- Competing for attachment sites/nutrients with the pathogens.

**Loperamide**
- Decreases the motility of the circular and longitudinal smooth muscles of the intestinal wall which increases the colonic transit time and amount of water absorption.
- Decreases colonic mass movements and suppresses the gastrocolic reflex.

**Atropine-Diphenoxylate**
- Atropine reduces spasms in the bladder, stomach, and intestines.
- Diphenoxylate acts by slowing intestinal contractions and peristalsis.

### Side Effects

**N.A**

Drowsiness, constipation, abdominal pain, dry mouth, fatigue, in rare cases toxic mega colon

stomach pain or bloating, fast heart rate, dizziness, stomach upset, loss of appetite.
HOW HEXBIO® HELP DIARRHEA???
Mechanism of Action

- Produce anti-microbial substances
- Reduce rotavirus shedding
- Secretes lactase enzyme

- Neutralize enterotoxins from pathogen
- Suppress the replication of virus
- Facilitate digestion of lactose

- Neutralize enterotoxins from pathogens.
- Produce anti-microbial substances to suppress the growth of pathogens.
- Reduce rotavirus shedding.
HEXBIO® & Constipation
**Pathophysiology of Constipation**

- **Low Fiber Diet**: Slows the rate of digestion.
- **Low Water Intake**: Increased colonic transit time.
- **Controlling the Urge**: Contraction of external sphincter and associated muscles.
- **Medical Condition**: Alteration of normal flora in the gut.
- **Low Physical Activity**: Low Metabolic rate.
- **Lifestyle Changes**: Sympathetic response.
- **Laxative Abuse**: Damaged nerve cells in colon.

- **Decreases bulk of the stool**.
- **Increased reabsorption of fluid**.
- **Absence of bowel movement**.
- **Decreased intestinal activity**.
- **Decreased peristalsis**.
- **Decreased intestinal motor activity**.
- **Decreased natural contracting ability**.

**CONSTIPATION**
Vulnerable Groups

- Aged Population
- Low Birth Weight Infant
- Stress
- Travelling Individual
- Bed Ridden Patients
- Medication
- Pregnant Mothers

- Laxative Abuse

- Pregnancy
- Medication
## Summary of Complications

<table>
<thead>
<tr>
<th>Vulnerable group</th>
<th>Symptoms</th>
<th>Ranking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed ridden patients</td>
<td>90%</td>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
</tr>
<tr>
<td>Post operative patients</td>
<td>20%</td>
<td>7&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stroke Patients</td>
<td>15%</td>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pregnant mothers</td>
<td>50%</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
<tr>
<td>Postpartum mothers</td>
<td>10%</td>
<td>4&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>Orthopedic patients</td>
<td>9.9%</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetic patients</td>
<td>26%</td>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Reference: Various
# 10 Principal Causes of Deaths in MoH Hospitals

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Heart Diseases &amp; Diseases of Pulmonary Circulation</td>
<td>16.54%</td>
</tr>
<tr>
<td>2</td>
<td>Septicaemia</td>
<td>13.18%</td>
</tr>
<tr>
<td>3</td>
<td>Malignant Neoplasms</td>
<td>11.21%</td>
</tr>
<tr>
<td>4</td>
<td>Pneumonia</td>
<td>9.28%</td>
</tr>
<tr>
<td>5</td>
<td>Cerebrovascular Diseases</td>
<td>8.65%</td>
</tr>
<tr>
<td>6</td>
<td><strong>Diseases of the Digestive System</strong></td>
<td><strong>5.18%</strong></td>
</tr>
<tr>
<td>7</td>
<td>Accidents</td>
<td>5.00%</td>
</tr>
<tr>
<td>8</td>
<td>Certain Conditions Originating in the Perinatal Period</td>
<td>3.97%</td>
</tr>
<tr>
<td>9</td>
<td>Nephritis, Nephrotic Syndrome and Nephrosis</td>
<td>3.76%</td>
</tr>
<tr>
<td>10</td>
<td>Ill-defined Conditions</td>
<td>2.63%</td>
</tr>
</tbody>
</table>
As it is showed above, colorectal cancer is the second highest with 13.2% out of ten most highest incidence of cancer in Malaysia. Colorectal cancer need to be given a higher attention as occurs more frequently among Malaysians in both male and female equally.
Bowel Movement (BM) Frequency and Risk of Colorectal Cancer in a Large Cohort Study of Japanese Men and Women

Above chart shows the average Incidence Rate Ratios (IRR) for colorectal and colon cancer according to BM frequency. As shown, it is the best to have BM 4-5 times a week as it shows the lowest IRR. Too often of BM per day can cause higher risk of colon and colorectal cancer. This is the same with BM every 6 days or less which has IRR of 1.81 average for both men and women.

British Journal of Cancer (2004) 90, 1397-1401
Above graph shows the frequency of stools during the study period of 7 days. According to the results, stool frequency increased from 1.4 (before treatment) to 4.3 (after treatment). This indicates the efficacy of Hexbio® in increasing patients’ bowel movement and reduces constipation.

Tan KB, Gee T, Romzi MA, Cheong JL, Department of Dietetics and Food Service, Hospital Kuala Lumpur
HOW HEXBIO® HELP CONSTIPATION??

- Secretes organic acids, maintaining acidic environment that induce peristalsis.

- Regularize bowel movement and shortens the Colonic Transit Time.
HEXBIO®

For
Nutrient Absorption, Immunity & Recovery
IMPROVE QOL

CLINICAL NUTRITION

ABSORPTION

HEXBIO®
HOW HEXBIO® HELP IN NUTRIENT ABSORPTION
Promote nutrient bioavailability by facilitating the breakdown of protein in native milk, which releases calcium and magnesium in higher concentration

- Production of important digestive enzymes, such as β-galactosidase
- Reduced cholesterol absorption
- Delayed gastric emptying
- Production of Vitamin Bs & K

HOW HEXBIO® HELP TO INDUCE IMMUNITY???
Mechanism of Action

Immunostimulation of mucosal membrane

Increase Synthesis of IgA
Increase T-Lymphocytes
Activate MDC

- Induces secretion of Immunoglobulin A
- Increase level of T-Lymphocyte cells as well as other helper immune cells
- Activate the human myeloid dendrite cell (MDC) to induce immune response
HOW TO USE?

WHEN TO USE?
## Dosage & Administration

### Recommended Dosage

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Adult Dose</th>
<th>Child Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic Microbial Diarrhea</td>
<td>2 sachets/day for 3 days</td>
<td>1 sachet/day for 3 days</td>
</tr>
<tr>
<td>Antibiotic Associated Diarrhea (after 3-4 hours of antibiotic)</td>
<td>2 sachets/day along with the course of antibiotics</td>
<td>1 sachet/day along with the course of antibiotics</td>
</tr>
<tr>
<td>Lactose Intolerance</td>
<td>2 sachets/day for 3 days</td>
<td>1 sachet/day for 3 days</td>
</tr>
<tr>
<td>Constipation</td>
<td>2 sachets/day for 5 days</td>
<td>1 sachet/day for 5 days</td>
</tr>
<tr>
<td>IBD</td>
<td>2 sachets/day for 4-8 weeks</td>
<td>1 sachet/day for 4-8 weeks</td>
</tr>
<tr>
<td>IBS</td>
<td>2 sachets/day for 4-8 weeks</td>
<td>1 sachet/day for 4-8 weeks</td>
</tr>
<tr>
<td>Maintenance</td>
<td>1 sachet/day when necessary</td>
<td>1 sachet/day when necessary</td>
</tr>
</tbody>
</table>

### Direction of Use
- Administer orally by pouring it directly into the mouth.
- Drink a glass of water
- Mix with water / juices / isotonic drinks / milk
- Consume immediately once sachet is opened

### Period of Administration
- Before or after meal

### Precautions
- Do not administer with antibiotics at the same time
- Do not consume with alcohol
Dosage

1. Oral Dose
Take 1 sachet during Breakfast & 1 sachet during Dinner by directly pouring into the mouth

2. Liquid Dose
1 sachet (3g) to 5ml water/juices/energy drinks/milk

Pour 1 sachet into 5ml water
Stir to mix
Feed using syringe / dropper
<table>
<thead>
<tr>
<th>Content</th>
<th>Unit</th>
<th>HEXBIO*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>gram per sachet</td>
<td>0.16</td>
</tr>
<tr>
<td>Fat</td>
<td>gram per sachet</td>
<td>0</td>
</tr>
<tr>
<td>Fiber</td>
<td>gram per sachet</td>
<td>0</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>gram per sachet</td>
<td>2.7</td>
</tr>
<tr>
<td>Calories</td>
<td>kcal per sachet</td>
<td>11.6</td>
</tr>
</tbody>
</table>

* Hexbio® is safe for all type of patients’ from all age group to consume, since the nutritional values are in the safe range.
STOOL ASSESSMENT & DIGESTIVE HEALTH
DEFECATION...
Is not evaluated according to
HOW MANY times we defecate..

It is evaluated according to the TYPES of stool that been eliminated..

Types of Stool
<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>3</td>
<td>Like a sausage but with cracks on its surface</td>
</tr>
<tr>
<td>4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>5</td>
<td>Soft blobs with clear-cut edges (passed easily)</td>
</tr>
<tr>
<td>6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>7</td>
<td>Watery, no solid pieces. Entirely Liquid</td>
</tr>
</tbody>
</table>

- **Constipation**
- **Normal**
- **Diarrhea**