Medical Foods

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The definition for a medical food is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles. It is established by medical evaluation. To be considered a medical food, a product must, at a minimum, meet the following criteria:

- The product is a food for oral or tube feeding
- The product is labeled for the dietary management of a medical disorder, disease, or condition, and
- The product is labeled to be used under medical supervision, and is primarily obtained through hospitals, clinics, and other medical and long term case facilities.

Classification

The classification of medical foods is relied on practical use for clinical indications providing general nutrition or specific metabolic needs:

1. Nutritionally complete formulas
   - 1.1 Polymeric formulas
   - 1.2 Predigested formulas
   - 1.2.1 Oligomeric formulas
   - 1.2.2 Monomeric formulas
   - 1.3 Disease-specific formulas
2. Nutritionally incomplete formulas or modular product
3. Formulas for metabolic (genetic) disorders

Polymeric formulas

Polymeric formulas are nutritionally complete diet and contain macronutrients in the form of intact carbohydrate, protein, and lipid which require functional digestive enzymes for assimilation.

Formula composition (Table 1)

- The energy derives from carbohydrate, protein, and fat as 40-60%, 12-20% and 30-40% of total calories. Mostly, these formulas contain 1 kcal/mL resulting to the osmolality ranged between 300 and 450 mOsm/kg.
- Carbohydrate is mainly composed of maltodextrin in the absence of lactose. Sucrose may be added to adjust palatability but this also increases osmolality. Some formulas contain starch.
- Protein content varies from 3 to 8 g/dL with a non-protein calorie:nitrogen between 75:1 to 150:1 kcal/g nitrogen. Sources of protein are whole intact proteins, which originate from natural forms (milk and egg protein) and protein isolates (casein, whey, and lactalbumin from cow's milk; soy protein isolate from soybean; egg white and egg albumin from eggs).
- Generally, vegetable oils providing long-chain triglycerides (LCT) such as soybean oil, corn oil, sunflower oil and safflower oil are the major sources of lipid in polymeric formulas. Medium-chain triglycerides (MCT) oil is occasionally added.
- Fiber is defined as carbohydrates that are normally indigestible in the human small intestine whereas they are fermented by colonic anaerobic bacteria. Fiber plays an important role as prebiotics to promote growth of normal flora or probiotics and also provides by-product from fermentation for colonic epithelial cell growth. Fructooligosaccharides (FOS), galactooligosaccharides (GOS), inulin, and gums are widely added as a part of dietary fiber. Oligosaccharides, such as FOS and GOS, and fructose polysaccharide, such as inulin containing 1 molecule of glucose and 60 molecules of fructose, are naturally occurring from chicory root, onion, artichoke, asparagus and banana.[2] Gums, a kind of polysaccharides, are obtained from oats, legumes, guar and barley. Whelan et al. found that, compared to standard enteral feeding formula, formula containing FOS and fiber significantly increased bifidobacteria and reduced clostridia in stool.[3]
- Micronutrients and trace elements usually meet 100% of the requirement when provided in adequate volume.

Electrolyte imbalances, osmotic diarrhea and dehydration may occur, therefore, monitoring should be performed while supplementation of these formulas despite being the nutritionally complete formulas.

Oligomeric formulas (Table 2)

Oligomeric formulas consist of peptides as major nitrogen source; a mainly combination of maltodextrin, sucrose, and occasionally, with lactose; a mixture of long-chain triglyceride with variable amounts of MCT; micronutrients and vitamins. Nitrogenous source is derived from enzymatic hydrolysis of whey or casein protein, which provides varying degree of peptides and some amino acids depending on partial or extensive degree of hydrolysis. These formulas have caloric density

ranged between 0.67 and 2 kcal/mL, which relies on susceptibility of gastrointestinal tract of patients at varied age groups. Clinical use of oligomeric formulas includes cow's milk protein allergy, and conditions of impaired digestion and malabsorption such as short bowel syndrome, inflammatory bowel disease, and pancreatic insufficiency. The characteristics of each formula should be taken into account to be appropriate for individual's age and medical condition.

Recommendation of American Academy of Pediatrics, Committee on Nutrition addressed that hypoallergenic formulas which include a free amino acid-based formula and extensively hydrolyzed formula, mainly containing free amino acids and peptides < 1,500 kDa, can be used as an alternative to breastfeeding in infants who develop symptom of food allergy.[4]

There was a study showing that early enteral feeding with oligomeric formula was well tolerated in adult patients with acute severe pancreatitis; septic and non-septic complications and cost of treatment were lower in enteral feeding compared to those of parenteral nutrition.[5]

Monomeric formulas

In monomeric formulas, nitrogenous source is in the form of free amino acids. Carbohydrates are glucose polymer in the form of starch and its hydrolysates in the absence of lactose. Lipids are provided by long-chain triglyceride from vegetable origin and medium-chain triglyceride. Compared to polymeric formulas, these formulas have some disadvantages such as higher osmolality, poor palatability due to amino groups of amino acids, and higher cost. Monomeric formulas are indicated for patients with severe cow's milk protein allergy (Table 3).

Disease-specific formulas

Disease-specific formulas, nutritionally complete diets, are modified by either decrease or increase some nutrients to meet the requirements of unique specific diseases or specific organs. There are special formulas available for liver disease, pulmonary disease, renal disease, and diabetes mellitus.

Hepatic failure formula

Patients with hepatic failure and hepatic encephalopathy have decreased levels of branched-chain amino acids (BCAAs: valine, isoleucine and leucine) but increased levels of aromatic amino acids (AAAs: phenylalanine, tryptophan, tyrosine) in plasma and cerebrospinal fluid. Consequently, AAAs can cross blood brain barrier and are the substrates of synthesizing false neurotransmitters causing hepatic encephalopathy. To correct the abnormal plasma ratio of these amino acids, the specialized formula containing a higher proportion of BCAAs relative to lowered AAAs is synthesized.

Pulmonary formula

Patients with respiratory failure who have a difficulty of weaning from a ventilator face with high CO_2 production; therefore, this special formula is designed by providing lipid content up to 55% in order to produce less CO_2. Meanwhile carbohydrate content in this solution is lessened.

Renal failure formula

Patients with renal failure have a markedly limited renal function to excrete toxic metabolites and minerals. Plasma levels of essential amino acids (EAAs) are increased, whereas those of nonessential amino acids (NEAAs) are decreased. Enteral nutrition for compromised kidneys is aimed to minimize blood urea nitrogen and creatinine, while maintaining water and electrolyte balance as well as providing optimal nutritional status. Pre-dialytic formula is energy-dense, low protein fortified with EAAs whereas formula for dialytic patients is caloric-dense, high protein. Moreover, fluid and electrolyte status need to be followedup.

Diabetes mellitus formula

Diabetes is highly associated with cardiovascular disease; therefore, controlling blood glucose and plasma lipid levels is necessary. The NCEP III guidelines address the recommendation of not only reducing dietary saturated fat intake to < 7% of total calories and cholesterol intake to < 200 mg/d but also increasing consumption of monounsaturated fat up to 20% of total calories to lower plasma LDL-C and cardiovascular disease risk in diabetes.[6] Enteral formulas for diabetes contain protein, lipid, and carbohydrate in amount of 15-20%, 30% and 50-55% of total calories, respectively. In brief, vegetable oil containing high oleic acid is used as a main source of lipid and polysaccharide remains a major part of carbohydrate. In some regimens, fructose is also added.

Compared with Average American diet, high-MUFA diets lowered total cholesterol by 10%, LDL-C by 14%, and triacylglycerol by 13%.[7] Another study showed the favorable effects of a reduced-carbohydrate, modified-fat with high-MUFA formula on markers of diabetic control and increasing serum HDL-C level in the absence of significant change in total cholesterol, LDL-C, and triacylglycerol.[8] Hawkins et al. demonstrated that administration of fructose was associated with decrease in glucose production in response to hyperglycemia in type 2 diabetic subjects, likely caused by impaired glucokinase activily.[9]

Modular diets

Modular diets, tailor-made formulas, contain macronutrients in combination with micronutrients prepared by mixing separate ingredients to modify the quantity or quality of contents to meet particular requirement of diseases. The source of carbohydrate is commonly derived from glucose polymer and those of protein include casein, whey, lactalbumin, egg albumin, or soy protein. Vegetable oil providing energy and essential fatty acids, and MCT oil have been considered as origins of lipid of these diets. Incompatibility and contamination should be taken into account when mixing is carried out.[10]

Our previous study reported that a ketogenic diet, tailor-made low-carbohydrate, high-fat regimen, was modified to be an additional therapy for refractory epilepsy and showed satisfactory outcome.[10]

Formulas for Metabolic disorders

There are formulas to support patients with specific inborn error of metabolism. A number of nutrients of these formulas are modified to be suitable for each disease such as urea cycle disorders (Protein-free formula; product 80056), maple syrup urine disease (BCAAs-free formula; product MSUD), and phenylketonuria (Phenylalanine-free formula; product PKU 1, PKU 2). Other nutrient deficiencies may occur in case of long term feeding with only the metabolic formulas, hence, proper nutritional supplementation and close monitoring should be taken into account depending mainly on the age of patient and severity of the disorder.

TABLE 1. Nutrient composition of polymeric formulas

Formula	Osmolality (mOsm/kgH_2O)	Caloric density (kcal/mL)	NPC:N (kcal/g nitrogen)	CHO g/dL (%kcal)	CHO Source	Protein g/dL (%kcal)	Protein Source	Lipid g/dL (%kcal)	Lipid Source	Na (mmol/L)	K (mmol/L)	Ca (mg/dL)	P (mg/dL)	Mg (mg/dL)	Fe (mg/dL)	Fiber (g/dL)
Nutren Optimum	350	1	121:1	12.84 (53)	Maltodextrin (48%) Corn syrup solid (34%) Sucrose (18%)	4.28 (17)	Whey (50%) Casein (50%)	3.5 (30)	Corn oil Canola oil MCT oil Soy lecithin	38.4	32.3	67.5	68.2	27.1	1.21	-
Nutren Fiber	360	1	133:1	12.76 (53)	Maltodextrin (51%) Corn syrup solid (29%) Sucrose (20%)	3.99 (17)	Whey (50%) Casein (50%)	3.78 (30)	Corn oil (18%) Canola oil (55%) MCT oil (27%)	38	33	67.9	67.3	26.7	1.21	1.3
Nutren Balance	NA	1	138:1	11.22	Potato starch (9%) Modified starch (91%)	3.83	Whey (50%) Casein (50%)	4.44	Sunflower oil (70%) Canola oil (25%) Soy lecithin (5%)	38	16	72.6	68.3	27.3	1.35	Arabic gum Yellow pea fiber Inulin } 1.52
Ensure	466	1	142:1	13.56 (55.3)	Hydrolyzed corn starch (37%) Maltodextrin (37%) Sucrose (26%)	3.7 (15)	Casein (80%) Soy protein isolate (20%)	3.26 (29.7)	Soybean oil (37%) Sunflower oil (63%)	36.5	40	127.2	127.2	42	1.92	FOS 0.83
Jevity	310	0.97	124:1	12.2 (52)	Maltodextrin (87%) Soy polysaccharide (13%)	4 (17)	Casein (100%)	3.4 (31)	Sunflower oil (48%) Canola oil (29%) MCT oil (19%) Lecithin (4%)	38.3	38	63	63	19	1.4	1.32
Nutren junior	300	1	191:1	13.68 (53)	Corn starch (32.4%) Maltodextrin (32.4%) Sucrose (35.2%)	3 (12)	Whey (50%) Casein (50%)	4.03 (35)	Sunflower oil (42%) Corn oil (7%) Canola oil (26%) MCT oil (20%) Soy lecithin (5%)	21	28	91.7	61.2	11.7	1.03	-
PediaSure Complete	310	1	185:1	10.95 (44)	Maltodextrin (70%) Sucrose (30%)	3 (12)	Whey (50%) Casein (50%)	4.97 (44)	Soybean oil (30%) Sunflower (HO) (50%) MCT oil (20%)	35	33	97	80	20	1.4	FOS 0.36
Pan-Enteral	320	1	183:1	10.7 (44)	Dextrin (50%) Sucrose (50%)	3 (12)	Casein (100%)	5 (44)	Soybean oil (52%) MCT oil (48%)	19	28	86	43	8	1	-

NA: not available

TABLE 2. Nutrient composition of oligomeric formulas

Formula	Osmolality (mOsm/kgH_2O)	Caloric density (kcal/mL)	NPC:N (kcal/g nitrogen)	CHO		Protein		Lipid		Na (mmol/L)	K (mmol/L)	Ca (mg/dL)	P (mg/dL)	Mg (mg/dL)	Fe (mg/dL)	Fiber (g/dL)
				g/dL (%kcal)	Source	g/dL (%kcal)	Source	g/dL (%kcal)	Source							
Peptamen	375	1	130:1	13.44 (53)	Potato starch (15%) Maltodextrin (58%) Sucrose (27%)	4.33 (17)	Partially hydrolyzed whey (100%)	3.41 (30)	Soybean oil (22%) MCT oil (73%) Soy lecithin (5%)	23	32	80	70	40	1.26	-
Peptamen junior	300	1	181:1	13.3 (55)	Potato starch (13.2%) Maltodextrin (63.6%) Sucrose (23.2%)	2.9 (12)	Partially hydrolyzed whey (100%) : Peptide MW 240-500 Da 25% 600-1,100 Da 18% 1,200-5,000 Da 39% > 5,000 Da 17% Free amino acids 1%	3.71 (33)	Soybean oil (25%) Sunflower (7%) MCT oil (62%) Soy lecithin (6%)	27.6	33.4	88.4	58.9	11.2	1.05	-
NAN HA 1	275	0.67	255:1	7.6 (45)	Maltodextrin (30%) Lactose (70%)	1.5 (9)	Partially hydrolyzed whey (100%) : Peptide MW 140-600 Da 18.8% 600-3,000 Da 63.2% 3,000-5,000 Da 11.8% 5,000-10,000 Da 4.8% > 10,000 Da 1.3% Free fatty acids 5%	3.4 (46)	Milk fat (2.6%) Sunflower oil (10.4%) Canola oil (19.6%) Palm olein (43.2%) Coconut oil (19.4%) Fish oil (1%) Mortierella alpina oil blend (3.8%)	7	17	38	20	4.5	0.8	-
Enfalac HA	300	0.67	247:1	7 (42)	Lactose (100%)	1.5 (9)	Partially hydrolyzed whey (60%) Partially hydrolyzed casein (40%)	3.7 (50)	NA	8.9	20	45	30	5.4	0.8	-
NAN HA 2	290	0.67	206:1	8.11 (48)	Maltodextrin (23%) Lactose (77%)	1.85 (11)	Partially hydrolyzed whey (100%) Peptide MW 140-600 Da 18.8% 600-3,000 Da 63.2% 3,000-5,000 Da 11.8% 5,000-10,000 Da 4.8% > 10,000 Da 1.3% Free fatty acids 5%	3.04 (41)	Milk fat (3.6%) Sunflower oil (10.5%) Canola oil (19.5%) Palm olein (45.8%) Coconut oil (19.4%) Fish oil (0.7%) Mortierella alpina oil blend (0.5%)	15	20	65	52	6.5	1.1	-
Pregestimil	320	0.67	198:1	6.9 (41)	Modified corn starch (25%) Corn syrup solid (75%)	1.9 (11)	Extensively hydrolyzed casein (100%)	3.8 (48)	Soybean oil (12.5%) Safflower oil (12.5%) Corn oil (20%) MCT oil (55%)	14	19	63	42	7.5	1.2	-
Nutramigen	320	0.67	198:1	7.4 (44)	Modified corn starch (20%) Corn syrup solid (80%)	1.9 (11)	Extensively hydrolyzed casein (100%)	3.4 (45)	Soybean oil (20%) Safflower oil (15%) Palmolein (45%) Coconut oil (20%)	14	19	63	42	7.4	1.1	-

NA: not available

TABLE 3. Nutrient composition of disease-specific formulas

Formula	Osmolality (mOsm/kgH_2O)	Caloric density (kcal/mL)	NPC:N (kcal/g nitrogen)	CHO		Protein		Lipid		Na (mmol/L)	K (mmol/L)	Ca (mg/dL)	P (mg/dL)	Mg (mg/dL)	Fe (mg/dL)	Fiber (g/dL)
				g/dL (%kcal)	Source	g/dL (%kcal)	Source	g/dL (%kcal)	Source	23	32	80	70	40	1.26	-
Hepatic failure formula Aminoleban oral	600	1	75:1	15.4 (60)	Dextrin (100%)	6.4 (25)	Casein (4%) Gelatin hydrolysate (48%) Free amino acids (48%) : BCAAs (45% of total AAs) : AAAs (7% of total AAs)	1.7 (15)	Rice oil (100%)	9.8	19.8	32.8	39.9	9.6	0.66	-
Pulmonary failure formula Pulmocare	475	1.5	125:1	10.6 (28)	Corn starch (46%) Sucrose (54%)	6.3 (17)	Casein (100%)	9.3 (55)	Corn oil (16%) Canola oil (62%) Coconut oil (22%)	54	44	54	100	42	NA	-
Renal failure formula Nepro	665	2	156:1	22 (43)	Hydrolyzed corn starch (82.4%) Sucrose (9.6%) FOS (8%)	7 (14)	Casein (100%)	9.6 (43)	Safflower oil (HO) (70%) Canola oil (30%)	37	27	137	70	21	1.9	FOS 1.56
Diabetes mellitus formula Glucerna	354	1	129:1	8 (33)	Soy polysaccharide (20%) Maltodextrin (62%) Fructose (18%)	4.2 (18)	Casein (100%)	5.6 (49)	Sunflower oil (HO) (90%) Canola oil (10%) - - MUFA 34.7% total energy - - PUFA 7.5% total energy - - SFA 4.4% total energy	40	40	72	72	28	1.3	Soy fiber 1.43
Glucerna SR	498	0.93	107:1	12.3 (47)	Soy polysaccharide (3.5%) Maltodextrin (50%) Fructose (23%) Maltitol (20%) FOS (3.5%)	4.6 (21)	Casein (100%)	3.4 (32)	Soybean oil (7%) Sunflower oil (HO) (93%) - - MUFA 24% total energy - - PUFA 5% total energy - - SFA 3% total energy	38.5	40	105	105	42	1.9	FOS 1.18

NA: not available, BCAAs: branched-chain amino acids, AAAs: aromatic amino acids

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