How Does the Access® Bar Work?

The Physiological Mode of Action

a paper by Lawrence C.H. Wang, Ph.D.,
Inventor of the Access Bar

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Dr. Lawrence C. H. Wang was born in China and grew up in Taiwan. He received his B.Sc. in 1963 from National Taiwan Normal University in Taipei, Taiwan. In 1967 he received his M.A. from Rice University in Houston, Texas, and in 1970 his Ph.D. from Cornell University in Ithica, New York. His training is in animal and human physiology, biochemistry, and pharmacology. After teaching at the University of Oregon in Eugene in 1969-70 he migrated to Canada and since that time has taught at the University of Alberta. He is currently a professor of physiology in the Department of Biological Sciences.

Dr. Wang's current research interests involve energy metabolism and temperature regulation and include exercise physiology, the enhancement of cold tolerance in man, hibernation and hypothermia, and the influence of herbal compounds (e.g. ginseng) on learning and memory, aging, exercise, and obesity. His publications include four patents, five books, and over 140 original scientific research papers in international journals. His research has received support from the Natural Sciences and Engineering Research Council, Medical Research Council, Canadian Heart and Stroke Foundation, Muttart Foundation, Alberta Heritage Foundation for Medical Research, Canadian National Defense, and two international pharmaceutical companies.

Dr. Wang is currently the North American Editor of the Journal of Comparative Physiology B, a prestigious international scientific journal. He is also a member of the editorial boards of the American Journal of Physiology, Cryobiology, and the Journal of Chinese Medicine. Dr. Wang has been invited to present scientific lectures in over 13 countries including Canada, the U.S., Australia, the U.K., France, Germany, Sweden, Belgium, Netherlands, Czechoslovakia, Taiwan, and China. He has also presented more than 70 popular public lectures to lay audiences.

Dr. Wang is an elected Fellow of the Academy of Sciences of the Royal Society of Canada (1993), the highest honor recognized by peers. He has been the recipient of the Alberta Science and Technology Leadership Award for Innovation in Technology (1992); the Gordon Royal Maybee Award from the Canadian Institute of Food Science and Technology (1992); the Prominent Immigrant Award in Research and Development, and in science, from Employment and Immigration Canada and Alberta Career Development and Employment (1992); the Killam Annual Professorship for excellence in research, teaching, and community services from the University of Alberta (1991-92); the Professor in Residence Award from the Alberta Heritage Foundation for Medical Research (1984-85); and the McCalla Professorships in Science from the University of Alberta (1983-84). Dr. Wang holds Visiting and Honorary Professorships in several prestigious Chinese universities: Peking Union Medical College, Jinan Medical College, Quingdao Medical College, and Xinjiang Medical College. Since 1995, Dr. Wang has been appointed as Presidential Advisor, International Affairs at the University of Alberta.

How Does the *Access* Bar Work?

(The Physiological Mode Of Action)

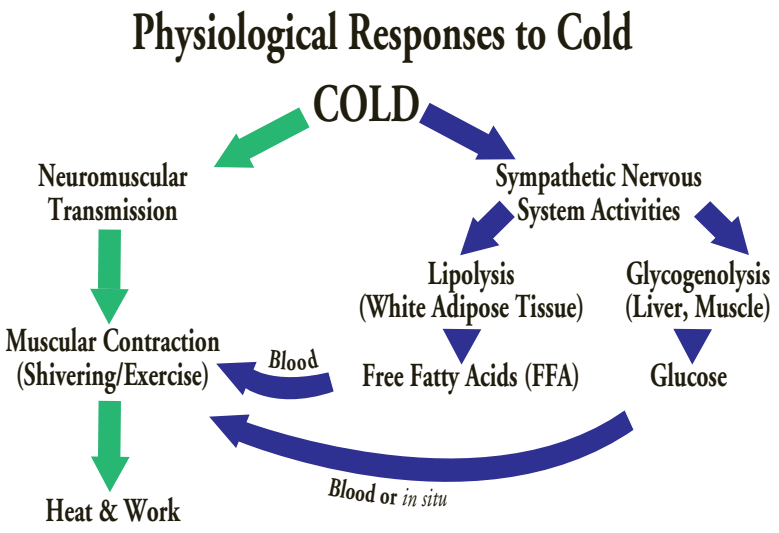

Diagram 1

Physiological Responses to Cold (Diagram 1)
Cold temperature stimulates the activity of the sympathetic nervous system (and other endocrine functions, such as the release of glucagons, growth hormone, and corticosteriods, but for simplicity's sake, these have not been included here because the end result of this endocrine activation is quite similar to sympathetic activation), leading to enhanced substrate conversion and mobilization [see Ref. 9, 10]. The main fuels for muscle are glucose and free fatty acids [11]. Cold also stimulates muscle contraction via the somatic nerves. Because muscle is typically only 25% efficient, heat is generated as a by-product each and every time muscle contraction occurs. In order to keep warm in the cold, muscular activity must continue [12]. Thus, how to optimize the physiological support to enable sustained, aerobic muscular activity becomes a critical consideration [13]. This is not only relevant to maintaining cold tolerance but also to sustaining exercise activity in general.

Formation of Adenosine (Diagram 2)
Adenosine is formed as a natural product of our own metabolism when the rate of ATP (the key energy currency of our body) usage increases to support neural transmission and muscle contraction [29]. Adenosine is formed after ATP is hydrolyzed through enzymic pathways involving both the cytosolic and membrane 5'-nucleotidase [29]. Once formed, adenosine diffuses out of the cell into the extracellular space due to its concentration gradient. There, adenosine may enter general circulation (blood) or exert local "pacarine or autocrine" effects on target cells which possess specific adenosine receptors [29].

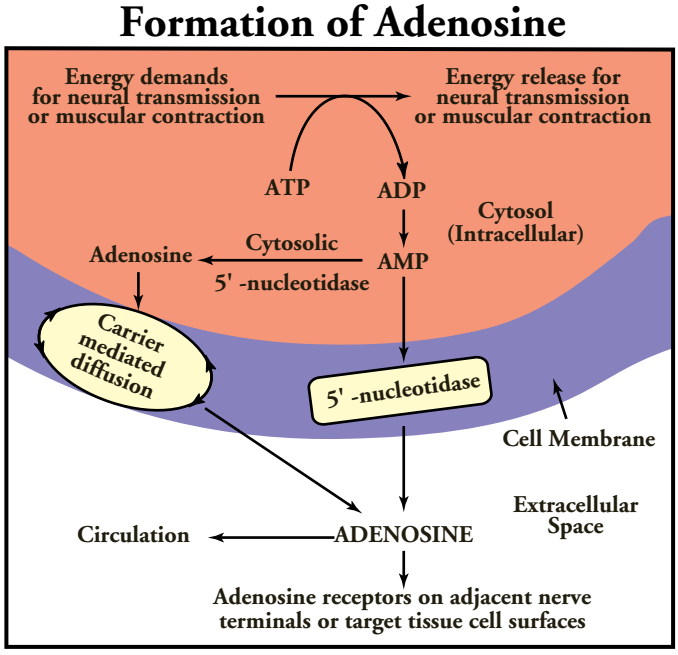

Diagram 2

Effect of Adenosine on Sympathetic Neurotransmission and Lipolysis (Diagram 3)
In the white adipocyte (fat cell), the conversion of stored fat into usable fat (fatty acids) requires the activation of an enzymatic reaction by cyclic AMP (cAMP) [14]. The formation of cAMP is enhanced by sympathetic activity via its neurotransmitter, norepinephrine (NE). Norepinephrine promotes the formation of cAMP from ATP by activating the membrane-bound enzyme adenylate cyclase [14]. Adenosine, on the other hand, exerts **negative** pre-synaptic modulation (via A1 receptors) on the postsynaptic release of NE [30]. Adenosine also inhibits the activity of adenylate cyclase via A1 receptors [26,29]. These combined effects effectively reduce the formation of intracellular cAMP, resulting in reduced conversion of stored fat to free fatty acids, which are required for sustained aerobic muscular contraction

Effect of adenosine on sympathetic neurotransmission and lipolysis

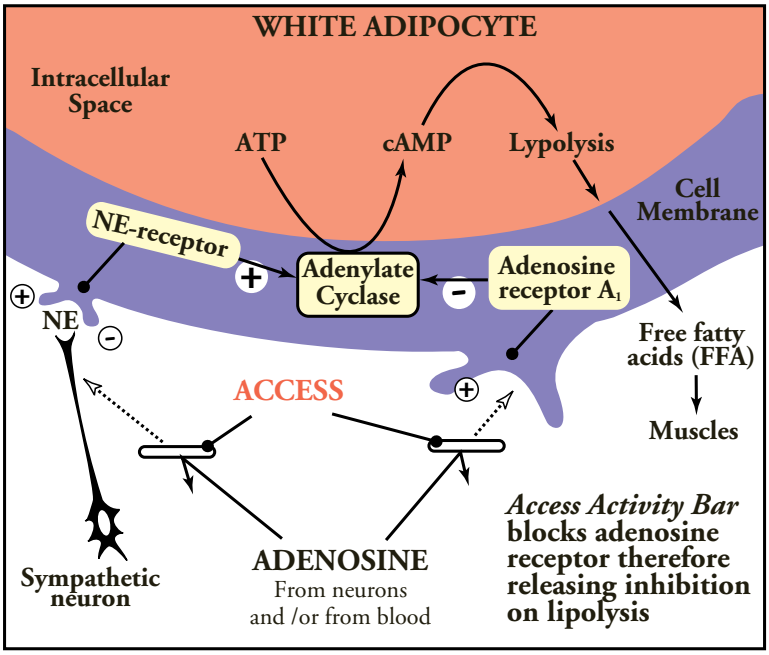

Diagram 3

[14-18, 25]. Physiologically-formed adenosine is hydrolyzed into inosine by the enzyme adenosine deaminase, and the half-life of newly-formed adenosine is short, typically less than one minute [29]. Thus, the action of adenosine is to serve as a pulsatile, negative feedback signal to reduce energy and fat consumption, being most prominent when the rate of ATP utilization is high, as in intense exercise. As energy and fat conservation serves to enhance survival in nature, the role of adenosine is considered to be adaptive, as energy procurement is often difficult and dangerous in nature [1-4,6-8]. The only exception is modern man, who now can procure energy at will without fear of predation. But adenosine's long-standing role in energy and fat conservation has still been retained; this causes a bottleneck whenever increased energy and fat consumption is desirable, such as during intense exercise activity. To circumvent this bottleneck, the negative effects of adenosine must first be overcome.

The adenosine receptor antagonists naturally present in the food ingredients of the *Access Bar* serve to **minimize** the negative impact of our own adenosine on energy and fat conversion [36]. The receptor antagonists can competitively block the adenosine receptors so that adenosine formed endogenously during activity can no longer bind to the same [19-24]. Meanwhile, adenosine is hydrolyzed by adenosine deaminase to inosine as normally occurs [29] but without first exerting its usual negative effect on fat and energy utilization. Consequently, fat conversion and fat utilization are increased to fuel our muscular activity. This "release of adenosine's inhibition" by the *Access Bar* is akin to the release of a hand-brake that had been left on in a fast-moving car; it now allows the body engine to fully exert its potential power to achieve peak performance. *Access* is certainly not a turbo-charger and it merely serves to release the innate power our bodies' "engines" possess in the first place.

Effects of Adenosine on Neuromuscular Transmission and Substrate Utilization (Diagram 4)

In the somatic nerve, adenosine also exerts pre-synaptic inhibition on the release of acetylcholine (Ach) [28,29,31], thus the neurotransmitter which elicits muscle contraction (i.e. aerobic exercise) can be limited. The *Access* Bar's natural adenosine-receptor antagonists can also release this inhibition and allow greater muscle recruitment, greater intensity, and longer duration of aerobic exercise.

Effect of adenosine on neuromuscular transmission and substrate utilization

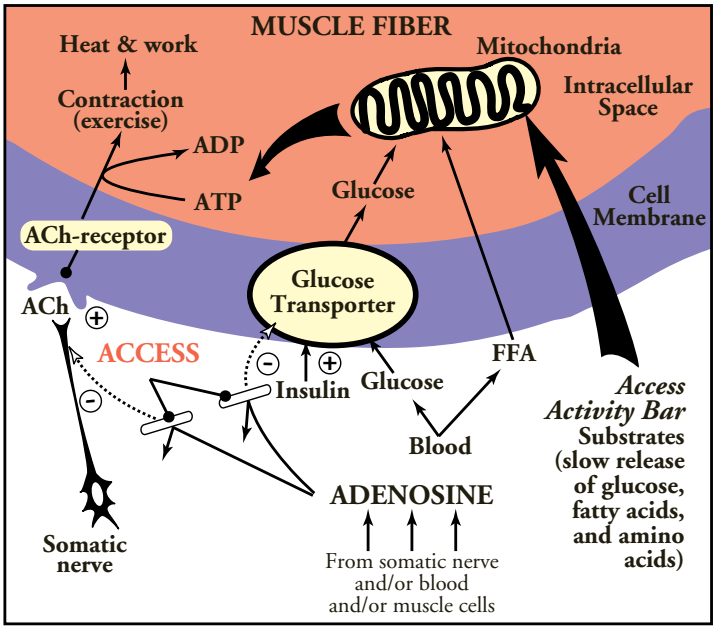

Diagram 4

Adenosine is also known to reduce the utilization of glucose by the muscle [27], although the precise mechanisms remain unclear; adenosine antagonists could also minimize this detrimental effect. The net benefits of these actions are that more active muscle fibers can participate in a given activity load, thus generating greater power. Further, with better fuel support, especially fat, the formation of lactic acid can be reduced and the onset of anaerobic threshold and fatigue can be delayed [34,35]. This will prolong the duration of intense activity and also reduce the recovery time due to less end-product accumulation.

Finally, the carefully-formulated proportions of protein, carbohydrate (simple, complicated, and complex forms), and fat in the *Access Bar* [this composition is patented, 36] allow a steady supply of optimal fuels to assist in the continued burning of fatty acids during aerobic activity. Because fat has to be burned in the "flame" of carbohydrates [5], the supply of a suitable amount of glucose (without being high enough to trigger the release of insulin) is critical in maintaining fatty acid utilization by the muscles. The proteins (amino acids) supply approximately 4-10% of the energy required in exercise and may assist in maintaining the smooth operation of the Tri-Carboxylic Acid cycle in the mitochondria for ATP production from glucose and fatty acids. The slow release of glucose, amino acids, and fatty acids may also contribute to the satiation effect after ingestion of the *Access Bar* because of the physiological action of these substrates on the hypothalamic satiety "center."

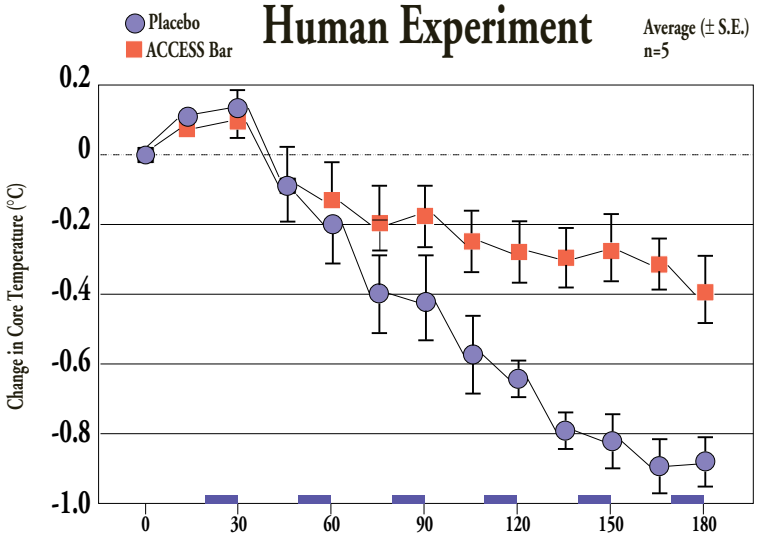

Diagram 5, Values Are Mean ± SE

Effects of *Access Bar* on Physical Performance in Man (Diagram 5, Values Are Mean + S.E.) The effectiveness of the *Access Bar* was double-blind tested in volunteers under conditions of moderate to strenuous physical activity [32-35]. Dressed in shorts (man) or shorts and a T-shirt (woman), each subject was exposed to -10 degrees Celsius with light wind (0.9 km/h) for three hours in a cold room and was asked to walk on a treadmill at a speed of 5-6 km/h one third of the time (10 min. walk, solid bars on diagram, 20 min. rest). Cold temperature alone caused the body to shiver (muscle contraction) to maintain warmth and this shivering alone raised the metabolic rate of the subject to 4-5 times of the resting level. This time-averaged rate over three hours was about 6.5 times of resting-akin to fast jogging and intense aerobic class activity. Eating an *Access Bar* at the 40-minute mark in the cold resulted in over 50% improvement in the final core (rectal) temperature, indicating significantly improved cold tolerance over when Placebo (non-caloric mixture) was given to the same subject for the same test and at the same time mark but one week apart. Since enhancement of cold tolerance depends on sustained aerobic heat production from the muscles through both shivering and exercise, it is evident that ingestion of *Access* has significant benefit in enhancing aerobic, sustained muscular activity.

How Different are the *Access Bar*'s Effects From Those of the Typical Commercial Chocolate/Snack Bars (Diagram 6, Values Are Mean + S.E.)

This is an important question because the ingredients of the *Access Bar* are seemingly typical of many other chocolate/snack bars. Before the U.S. patent was issued [36], this was exactly the same question raised by the U.S. Patent & Trademark Office. The U.S. Patent Office specifically challenged our application with a Japanese Patent disclosed in 1986 by Ogawa et al. on the teaching of composition and processing of a typical, generic chocolate mix (Jpn.Kokai Tokyo Koho JP 61,212,244). We had to demonstrate to the satisfaction of the U.S. Patent Office that the composition and functional usefulness of the *Access* Bar formulation was drastically and critically different enough to warrant consideration of patentability. To prove our point, we had to conduct a series of animal experiments comparing the Ogawa et al. formulation vs. ours in enhancing performance.

Using laboratory white rats, each was fed with either water or a nutritional mixture (Ogawa or *Access* formula, isocaloric to each other) and exposed to cold (-10 degrees Celsius) for up to three hours (very much like in our human experiments described above). The aerobic heat production reflected by oxygen consumption and carbon dioxide production was continuously monitored until a critical minimum level (1 Kcal/rat/15 min.) was reached, indicating the inability of the rat to continue enduring cold. The rectal temperature was then measured after the removal of the animal from cold and the duration of cold endurance recorded. As can be seen from Diagram 6, the Aerobic Intensity was least in water-fed, intermediate in Ogawa's cocoa mixture, and highest in *Access* mix. The difference between *Access* and Ogawa was highly significant statistically. Similarly, the Endurance to Cold Exposure was significantly higher after *Access* mix than the Ogawa and water. Further, the final core temperature was also significantly higher after *Access* mix than either Ogawa or water and again there was no difference between Ogawa and water treatment.

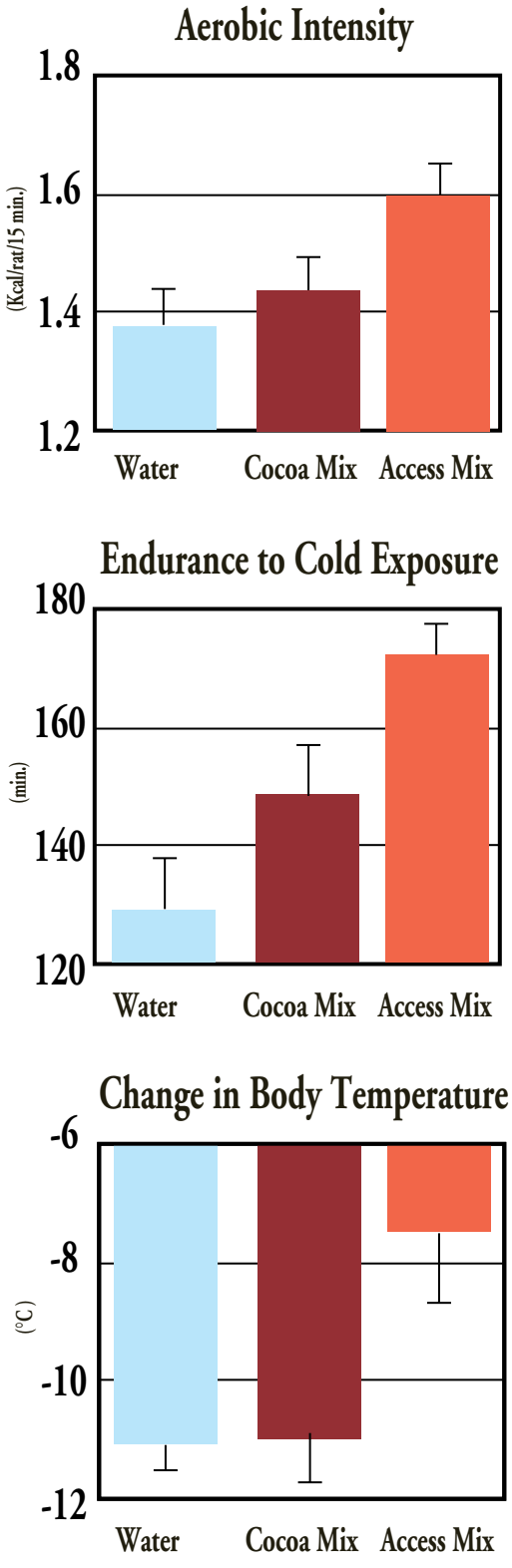

Diagram 6, Values Are Mean ± SE

This series of experiments has clearly demonstrated the following: a) the "generic" chocolate/cocoa mix, despite its high energy content (16 Kcal/5ml fed), has very limited physiological value in enhancing cold (aerobic) endurance vs. water alone (0 cal/5ml fed); b) although the *Access* mix contained exactly the same amount of energy (16 Kcal/5ml fed) as the "generic" mix, the physiological attributes in enhancing cold (aerobic) endurance and aerobic intensity are significantly better in *Access*; and c) it is therefore apparent that it is not the total amount of energy or calories contained in a nutritional bar or mix that is important, rather, it is how the calories are proportionated amongst the nutrients that is critical. With this demonstration of criticality in function the ***ACCESS FORMULATION*** was accepted by the U.S. Patent and Trademark Office as possessing truly **NOVEL AND UNEXPECTED FUNCTIONAL USEFULNESS** in enhancing aerobic performance, and warranted the patent protection [36].

IN SUMMARY, the *Access Bar*, being a relatively low-caloric product (140 Kcal) can exert a surprisingly high degree of energy enhancement for physical activity. The physiological secret is that it helps the burning of one's stored fat, a metabolic reserve which is typically not in shortage among the general population. As even the mildest exercise would require several hundred Kcal, the caloric content of the *Access Bar* is obviously insufficient to meet such a demand. The fact that each *Access Bar* can help one sustain intense activity for two hours or longer is clear indication that stored fuel (fat, in particular) must have been accessed in such an endeavor. When fat can be burned to sustain exercise, and when hunger pains can be alleviated after eating the *Access Bar*, physical activities beneficial to health and vitality can be practiced with greater ease and enjoyment. In the long term, the reduction of excess risks of obesity results in an even greater enhancement in the quality of life.

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