

Adenosine 5'-Triphosphate Disodium

Introduction

TSI holds an exclusively licensed suite of issued patents and patent-pending applications for the oral administration of adenosine 5'-triphosphate (ATP). Research conducted by Dr. Eliezer Rapaport, a widely recognized expert in adenosine nucleotides; TSI; and independent researchers, has convincingly demonstrated that ATP, as PEAK ATP®, can effectively elevate ATP levels in blood and tissues and increase circulation. Its ability to be absorbed into the bloodstream and provide maximum bioavailability is, however, dependent upon selecting specific application forms and applying the necessary corresponding technologies. This document outlines the advantages and drawbacks of today's most apt delivery systems.

**Enteric Coated
Tablets, Capsules and
Softgels**

- *Ideal way to maintain stability of PEAK ATP*
- *Generally accepted delivery form by consumers*

Absorption of nutritional components – whether from foods or dietary supplements – occurs largely in the duodenum, the proximal part of the small intestine. In order to make it to the duodenum intact, these components must survive the highly acidic environment of the stomach, which has a pH of about 1-2, and an average passage time of 30-120 minutes. Certain compounds, such as PEAK ATP, are not completely chemically stable in this acidic environment. Therefore, enteric coating is an ideal way to maintain the stability of PEAK ATP in the form of tablets, two-piece hard shell capsules and soft gelatin capsules.

Enteric coating is a manufacturing process that surrounds the tablet or capsule with materials that dissolve at a pre-determined pH higher than that of the stomach. An enterically coated PEAK ATP supplement would therefore pass through the stomach intact, be incorporated into the liquefied chyme (a mixture of partially digested food and gastric juices) and move on to the duodenum. Only there, where the pH reaches about 5-5.5, would the coating dissolve, releasing the contents and allowing rapid absorption through the intestinal wall into the portal circulation, and from there into the liver and then the bloodstream.

The advantages of enteric coated supplements are their general acceptance by consumers and their convenience. Disadvantages include the need to be taken on an empty stomach (one hour before a meal or two hours after) as well as determining the transit time of the dosage forms. Because a tablet needs to have binders, fillers and stabilizers, it takes longer to break down and absorb the active ingredient than with a liquid suspension. Capsules are dissolved more quickly, however they are still not as immediately absorbed as liquid formulations. Soft gelatin capsules (softgels), inherently delivering a liquid, offer the quickest absorption amongst the solid dose delivery forms, but the special skills and equipment needed to produce them with a fixed and uniform coating limits the number of companies able to offer them.

**Powders
(reconstituted in
water and drunk as
beverages)**

- *Attractive solution for those who have difficulty swallowing*
- *More rapidly absorbed than solid dose delivery forms*

Another delivery form for PEAK ATP, which is highly soluble, is as a powder that would be mixed with water and drunk as a beverage. An attractive property of a powder transformed into a liquid solution is rapid gastric passage and absorption, which is only about 15-30 minutes when taken on an empty stomach. The empty stomach is important, because if food is in transit, the highly acidic chyme and the stimulation of catabolic enzymatic activities in the duodenum could partially destroy the active ingredients. However, in the absence of liquefied chyme, a liquid solution of PEAK ATP would mostly be emptied into the duodenum and absorbed into the portal circulation, followed by first passage incorporation into the liver.

The advantage of this delivery system is rapid absorption, which could be particularly beneficial to competitive athletes. Powders also present an alternative for those who do not like to swallow tablets or capsules. The disadvantage of a powder is that many people do not have the patience to mix it themselves.

Orally Disintegrating Tablets (ODT)

- *Market research reveals that a significant % of consumers prefer ODTs to conventional solid dose delivery forms*
- *Quick, convenient and easy to use*
- *Prototype consumers have reported rapid onset of action and perceptible alertness*

Developing new and easier ways to consume products increases user interest, compliance and satisfaction. Orally Disintegrating Tablet (ODT) technology offers consumers a solid oral dosage form that can be swallowed without water because it starts dissolving on contact with saliva. The resulting liquid solution enables rapid gastric absorption, which too, is estimated at about 15-30 minutes when taken on an empty stomach. While this dosage form is intended for ingestion (it is not a sublingual), its innate properties will cause some of the active material to come in contact with the oral cavity tissue and be absorbed through the mucosal membranes into the bloodstream.

The major advantages of this delivery system are convenience and ease of administration, making it an ideal application for a wide range of consumer demographics and indications. Oral sensation preferences may be the only disadvantage of this technology, but taste-masking agents, flavors and sweeteners can be incorporated, which makes this delivery form highly attractive.

As of the writing of this document, TSI has only prototyped this novel delivery form to gauge consumer response, which has been vastly positive. Users report rapid onset of action and a perceptible increase in alertness. TSI has not conducted any stability and/or efficacy studies, nor has it fully optimized development work.

Liquid Beverages

- *Convenient, portable solution*
- *Rapid absorption*
- *Stable if prepared with a strong buffer*

A final option for PEAK ATP delivery is a prepared liquid beverage. The advantage of this delivery system is rapid absorption. Plus, beverages are convenient, single-serving packages that are portable and ready to drink.

PEAK ATP added to a beverage with a low pH would not be stable. However, the pH of the solution could be adjusted by using a strong buffer. If the liquid itself had a pH of 4.5 or above, the active material would be protected from gastric acidity without the use of enteric coating.

However, while gastric stability would not be an issue, on-shelf stability might be. That's because the chemical degradation that occurs in a low pH environment, such as the stomach, is different than the chemical degradation that occurs at room temperature. Whereas high acidity breaks down the adenine-ribose bond and renders the molecule completely inactive, degradation at room temperature over a period of months simply yields end products of ADP and AMP. These end products are also active in producing the desired effects of expanding blood plasma circulatory ATP pools. Therefore, while liquid beverages may not contain any ATP after months of sitting on the shelf, they could still be expected to provide some benefit.

TSI has conducted bench-scale and commercial-scale tests to determine the feasibility of stabilizing PEAK ATP in a conventional (high temperature / short-time pasteurization, low pH, and stabilized with antimicrobials) ready-to-drink beverage.

The feasibility appears promising; however, TSI does have concern that other ingredients in the customer's formula could be incompatible with ATP, thus affecting its stability and/or efficacy of the product itself.

Summary

TSI works closely with all our marketing and manufacturing licensees to ensure our PEAK ATP is stable in the final consumer product. In addition, we're committed to providing marketing and technical service support so that labeling materials reflect our brand's essential elements and accurate information.

PEAK ATP demonstrates TSI's ongoing commitment to developing and providing superior quality, well-researched ingredients that are proprietary in nature whenever possible, whereby offering our partners a significant advantage in bringing sound, efficacious products to market.

To incorporate PEAK ATP in your next product and set it apart from the competition, contact us today.

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