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Short Communication

Halomonas is becoming a Safe and Reliable Industrial Platform for Chemical Production

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DESCRIPTION

The shift from chemical-based products, which depend on fossil resources, to bio-based products is well underway in the manufacturing of chemical products. Contrary to chemical production processes, fermentation-based production does not use a catalyst or solvent, and all raw materials for fermentation are bio-based materials or nutrients salt. In the health food sector, both synthetically produced and bio-fermented health products are concurrently available in the market. Examples include amino acids and β-hydroxybutyric acid. However, the momentum for the shift chemical produced products to bio-based ones is growing year by year [1]. Extremophilic bacteria, especially halophiles, have received considerable attention owing to their unique properties; they can be used in applications requiring contamination-free culturing and high-substrate concentrations in industrial chemical production [1,2].

Members of the *Halomonas* genus have been isolated from various saline habitats such as salt lakes, marine environments, soils, salters, seafood, fermented salty food, and the culture medium of microalgae [3,4]. *Halomonas* strains are generally salt-tolerant and alkali-tolerant, thus they do not require medium sterilization for their culture, for most bacterium cannot grow such extremophilic condition, even some *Halomonas* sp. can grow with sea water [5,6]. Salt-tolerant bacterium has one another advantage for industrial utilization, namely the bacterium can use high carbon source concentration to lead high product concentration. Generally, most microbes can use carbon source at most 10% in batch culture system. In *Halomonas* case, 260.0 g/L of sucrose was used and obtained the total weights of the dried cells and PHB were 132.4 and 110.5 g/L, respectively [4]. They are fairly high productivity and conversion rate compared to chemical process; even they are cultured under aerobic fermentation condition. In addition, *Halomonas* strains can use agricultural residue directly such as biodiesel waste glycerol and saccharified wood to produce Poly-D-β-Hydroxybutyric acid (PHB) [7,8].

An alkaliphilic and halophilic bacterium, *Halomonas* sp. KM-1, has been isolated and found to store the bioplastic PHB intracellularly under aerobic conditions, and secretes D-B-Hydroxybutyric acid (D-BHB) under microaerobic conditions, pyruvic acid and oxaloacetic acid under aerobic condition with no genetic modification, just with culture condition control [7,9-11]. Recently, D-Beta-Hydroxybutyric acid (D-BHB) (OKETOA™) commercial production using the KM-1 was started by Osaka gas chemical. The D-BHB was attracted much attentions as the health food to improve the symptoms of disorders such as Alzheimer's disease, diabetes, cancer, anti-aging, and has been found to suppress myocardial infarction, improve motor function, and prevent the development of dementia, obesity, and migraine [4,12].

In market, two types of β-Hydroxybutyric acids were sold now, one is DL-Beta-Hydroxybutyric acid (DL-BHB) which was produced by chemical process as racemic form, and the other is D-BHB which was produced by fermentation process as natural from. Most of intracellular BHB is D-BHB, and and L-Beta-Hydroxybutyric acid (L-BHB) metabolic pathway and its intracellular activity is not apparent, thus at least in health food market, pure fermented D-BHB is preferred as more active form than racemic DL-BHB.

Due to the use of natural microorganisms without genetic modification and the lack of toxin-encoding genes in their genomes, it is believed that all impurities produced during fermentation, such as proteins, amino acids, pigments, and other compounds, are safe for consumption. The genome of *Halomonas* strains including the KM-1 does not contain toxin-encoding genes. Therefore, *Halomonas* strains are considered as a safe and its use in D-BHB and other chemical production is considered a safe process.

Recently, for the further safety confirmation, Katsuya et al., reported the safety of *Halomonas* sp. KM-1-derived D-BHB and the impurities generated during D-BHB manufacture at a 100-fold higher concentration by acute test using mouse, and daily intake of sixteen-gram D-BHB in Japanese adult for 12 weeks were investigated [4]. Therefore, the safety of *Halomonas* sp. KM-1 is further enhanced, and along with *Halomonas* advantages over varieties of industrial microorganisms, *Halomonas* strains

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KM-1 is further enhanced, and along with *Halomonas* advantages over varieties of industrial microorganisms, *Halomonas* strains could become a hopeful microbial platform to support future bio-based product manufacturing.

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