S-adenosylmethionine (SAM)

S-adenosylmethionine (SAM) is the major methyl donor for enzymatic methylations of various biopolymers in the cell,and also in the enzymatic capping process for mRNA vaccines and therapeutics. SAM is a chiral substance with two isoforms: (S,S)-SAM and (R,S)-SAM, and only (S,S)-SAM is biologically active.

Yeasen has devoted to be a leader in the manufacture and supply of mRNA raw materials (including the enzyme, NTP, SAM, etc) for quickly and successfully developing mRNA therapeutics and vaccines. Critical mRNA raw material considerations include the quality, flexibility, scalability, consistency, proven products, and regulatory support. To meet the critical requirements, Yeasen offers the SAM product conformed the following specification and attribute.

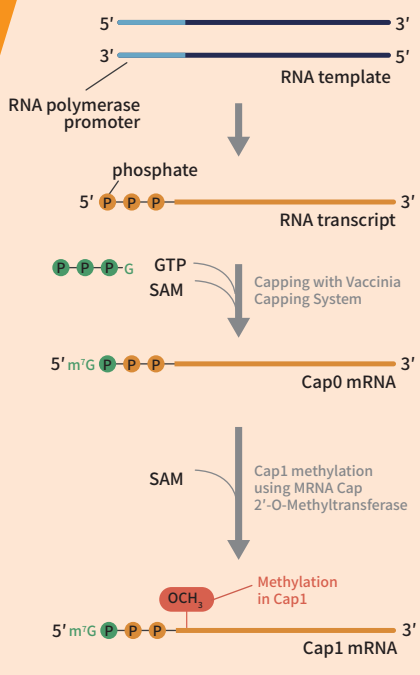


Figure 1. Enzymatic capping process

Specification

Item	Standard
Hazen/AHPA	Colorless to light yellow solution
Purity (HPLC)	⩾90%
ee (%) *	Conform
Concentration	32 mM±2 mM
Restriction Digest (CpG Resistant)	Pass
Exonuclease	Pass
Nickase	Pass

* Internal control items

Attribute

- Validated, product-specific process and analytical methods
- Product-specific stability
- Documentation follows applicable GMP guidelines
- AOF production process and raw materials (TSE & BSE)
- Nitrosamine statement
- Regulatory support documents available
- Large-scale production (10+ liter / Batch)

Purity Assessment

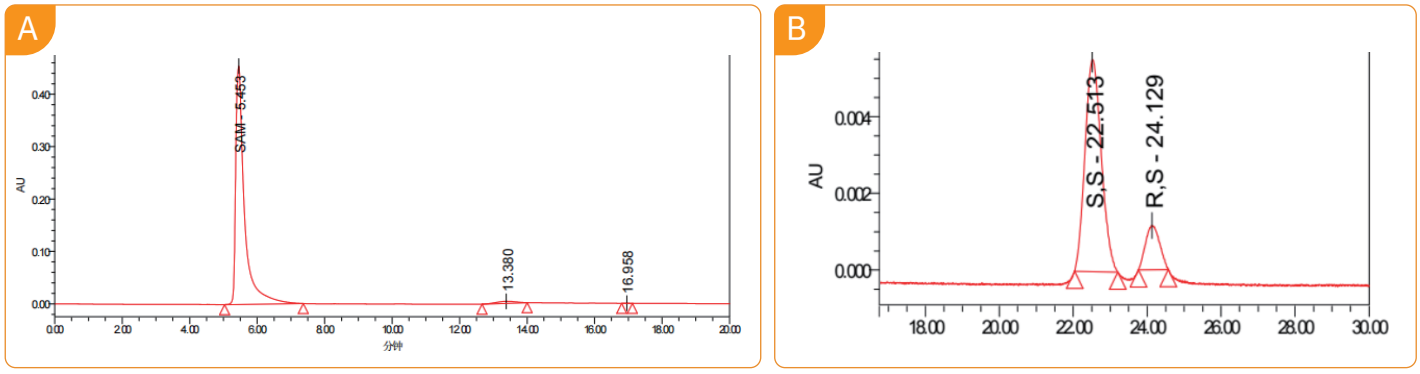


Figure 2. The purity (HPLC) of SAM product could be over 98% (A) and the optical purity (ee) of (S,S) -SAM isoform always be about 70% (B).

Enzyme Residual Detection

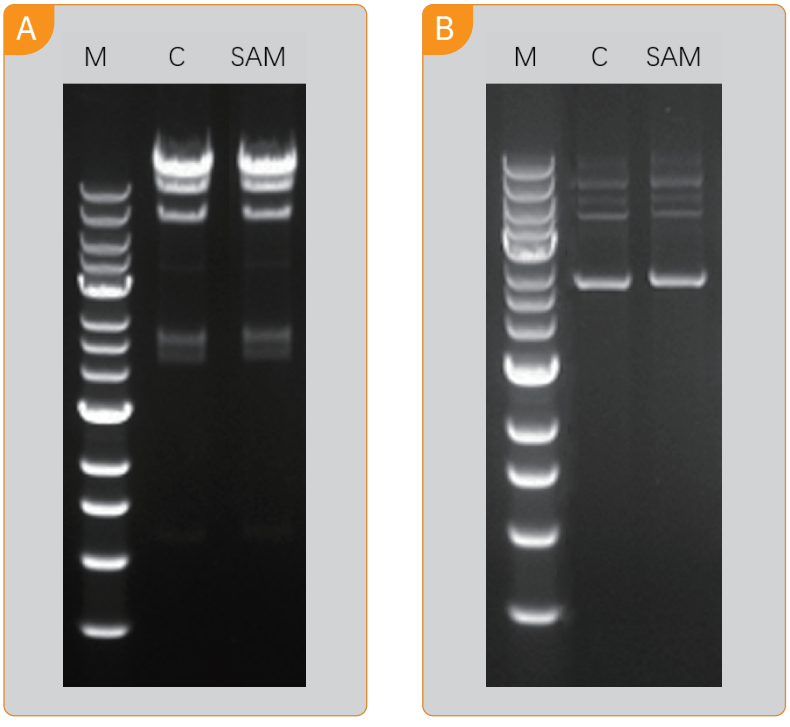
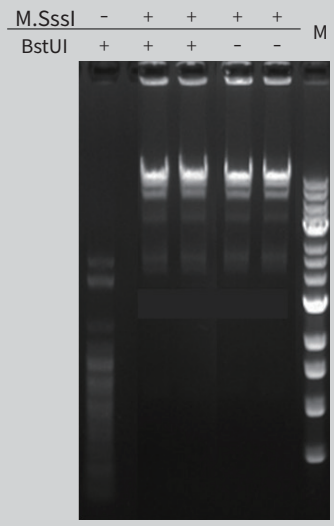


Figure 3. No enzyme residue was detected by agarose gel electrophoresis. A 20 µl reaction in the buffer containing 500 ng of Hind III digest of λDNA and 2 µl of S-adenosylmethionine (SAM) incubated for 4 hours at 37°C results in no difference compared with the control (SAM free in the reaction system) by agarose gel electrophoresis (A). A 20 µl reaction in the buffer containing 500 ng of pUC19 plasmid and 2 µl of S-adenosylmethionine (SAM) incubated for 4 hours at 37°C results in no difference compared with the control (SAM free in the reaction system) by agarose gel electrophoresis (B).

Functional Test and Verification

A



B

Component	20 µL Reaction	Final Concentration
Denatured RNA	10 µg	0.5 µg/µL
10× Capping Buffer	2 µL	1×
GTP (10 mM)	1 µL	0.5 mM
SAM (10 mM)	1 µL	0.5 mM
Murine RNase Inhibitor	20 U	1 U/µL
Vaccinia Capping Enzyme	50 U	2.5 U/µL
2´-O-Methyltransferase	50 U	2.5 U/µL
RNase-free H_2O	Up to 20 µL	-

C

Result	Cap1	Cap0	G-Cap	pp-RNA	ppp-RNA
Percentage (%)	99.03	0.21	0.14	0.62	0

Figure 4. The capping efficiency of Yeasen post-transcriptional capping reaction could be close to 99%. A 20 µl reaction in the buffer containing 1 µg of λDNA, 1 unit of M. SssI (CpG Methyltransferase), and 160 µM S-adenosylmethionine (SAM) is incubated for 1 hour at 37°C. The resulting DNA is resistant to digestion with BstUI as determined by agarose gel electrophoresis(A). 10 µg RNAs were denatured by incubation at 65°C for 5 min before capping. A 20 µL post-transcriptional capping reaction was set up according to the table (B) and incubated at 37°C for 2 hours in a PCR machine. Transcripts were purified by magnetic beads (RNA Cleaner, Yeasen#12602). Then the capping efficiency is detected by LC-MS (C).

Order Information

Product Name	Catalog No.	Size
S-adenosylmethionine (SAM) GMP-grade (32 mM)	10619ES02	0.5 mL
	10619ES25	25 mL
	10619ES50	50 mL
	10619ES76	500 mL

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