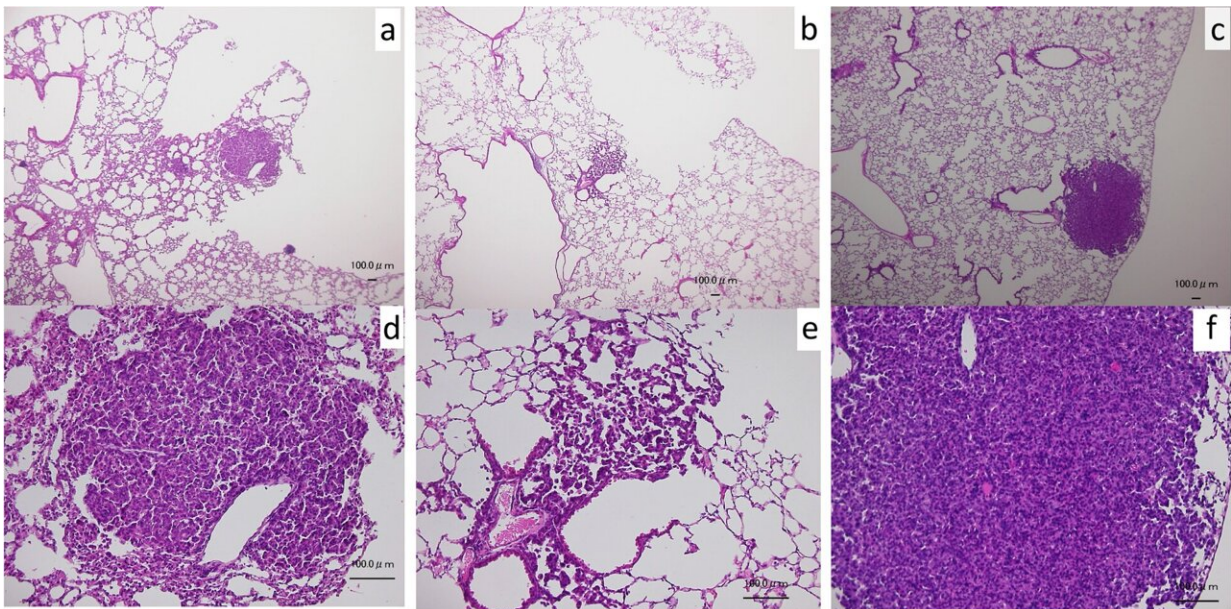


Actinidia arguta (sarunashi) juice found to inhibit lung cancer in mice

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A representative tumor (adenoma/adenocarcinoma) corresponding to the nodule counted macroscopically and the alveolar area around the tumor in the A/J mouse at 30 weeks of age treated with NNK alone (group I) (Fig. 1a). NNK + sar-j (group II) (Fig. 1b), or NNK + isoQ (group VI) (Fig. 1c) stained by Hematoxylin and Eosin. Figure 1d, e and f stand for the high magnification of the tumor in Fig. 1d, e and f, respectively. Bar. 100 µm. Credit: *Genes and Environment* (2022). DOI: 10.1186/s41021-022-00255-0

Lung cancer is a leading cause of death in Japan and across the globe. Among all the cancers, lung cancer has one of the lowest five-year

survival rates. Smoking tobacco and using tobacco-based products is known to heavily contribute to the development of lung cancer. It is a clinically established fact that the active ingredients in various fruits minimize the risk of chronic diseases including cancer.

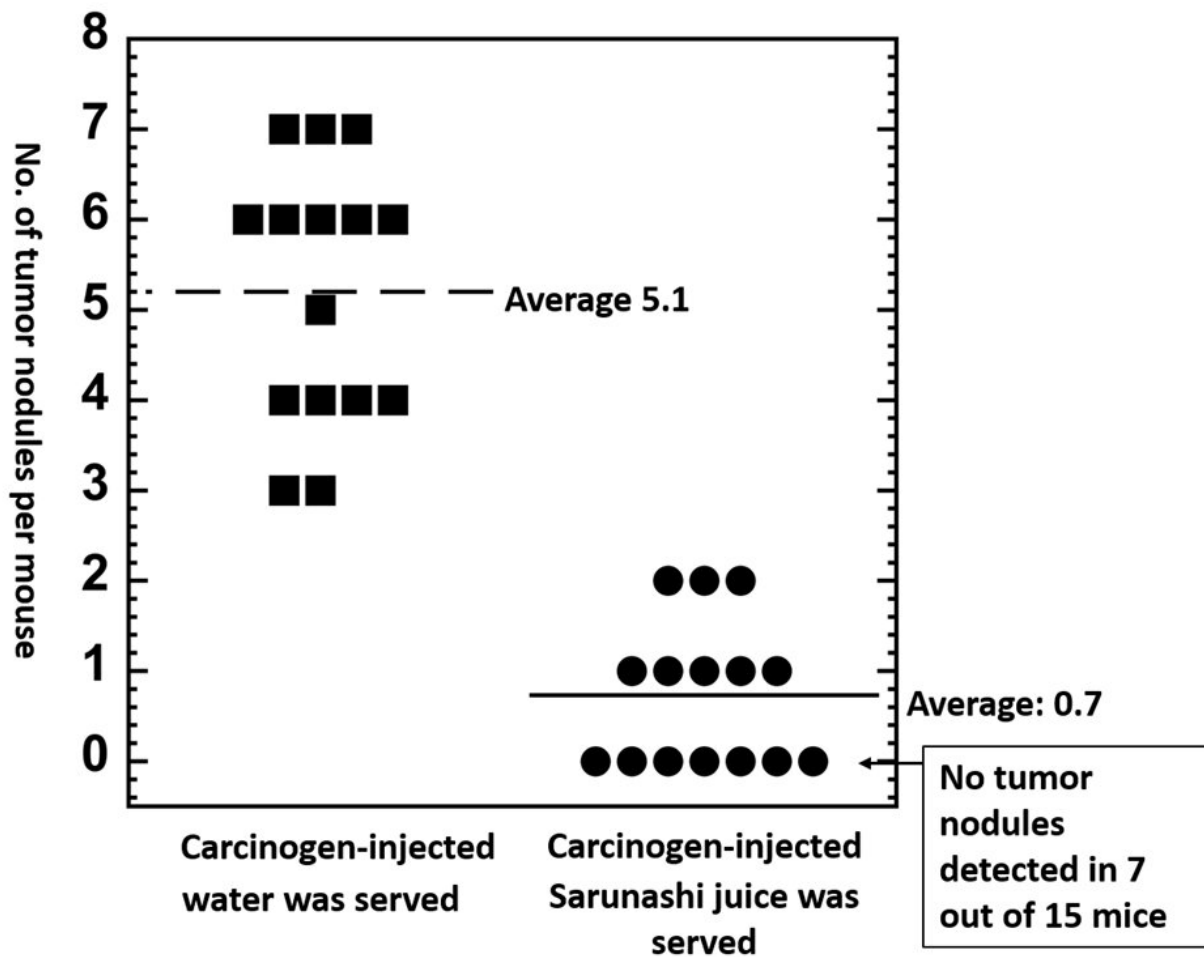
"Sarunashi" (*Actinidia arguta*) is an edible fruit cultivated in Japan's Okayama Prefecture. Using a [mouse model](#), researchers from Okayama University led by Dr. Sakae Arimoto-Kobayashi, Associate Professor in the Faculty of Pharmaceutical Sciences, Okayama University, have shown that sarunashi juice and its constituting component isoquercetin (isoQ) help prevent and reduce [lung cancer](#).

A. arguta is one of the richest sources of polyphenols and vitamin C. Previously, the researchers had demonstrated the inhibitory effect of sarunashi juice (sar-j) on mutagenesis, inflammation, and mouse skin tumorigenesis. They had identified the components of *A. arguta* responsible for the anti-mutagenic effects as water-soluble and heat-sensitive phenolic compounds. Subsequently, the researchers proposed the polyphenolic compound isoQ as a constituting component with anticarcinogenic potential.

Dr. Arimoto-Kobayashi explains, "In this study, we sought to investigate the chemo-preventive effects of *A. arguta* juice and its constituting component isoQ on 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced lung tumorigenesis in A/J mice, and identify the possible mechanisms underlying the anti-tumorigenic effects of *A. arguta*."

To this end, the team induced [tumor growth](#) in mice using NNK, a known cancer-causing compound present in tobacco products. Using a series of experiments and controls, the team studied the effects of sar-j and isoQ on lung tumorigenesis in mice.

The results were encouraging: The number of tumor nodules per mouse lung in the group that received NNK injections and oral doses of *A. arguta* juice was significantly lower than that in the group injected with NNK only. Moreover, the oral administration of isoQ also reduced the number of nodules in the mouse lungs.



In a study by researchers from Okayama University, *Actinidia arguta* (sarunashi) juice reduced tumor nodules in carcinogen-exposed mice. Credit: Sakae Arimoto-Kobayashi

Next, the team broke ground by discovering the likely mechanism of action. NNK and 1-methyl-3-nitro-1-nitrosoguanidine or "MNNG" are known mutagens—agents that trigger DNA mutations. The team therefore designed a series of experiments to study the effect of sar-j and isoQ on NNK- and MNNG-mediated mutagenesis using *Salmonella typhimurium* TA1535—a bacterial strain commonly used for detecting DNA mutations.

As expected, the mutagenicity of NNK and MNNG detected using *S. typhimurium* TA1535 decreased in the presence of sar-j. However, when similar tests were conducted using *S. typhimurium* YG7108, a strain lacking key enzymes responsible for DNA repair, sar-j was unable to decrease the mutagenic effects of NNK and MNNG. Based on this critical observation, the researchers concluded that sar-j seems to mediate its antimutagenic effect by accelerating DNA repair.

Finally, using cell-based experiments, the team also showed that sar-j suppressed the action of "Akt," a key protein involved in cancer signaling. It is a known fact that Akt and an associated protein called "PI3k," get over-activated in several human cancers.

Co-author Katsuyuki Kiura, a Professor in the Department of Allergy and Respiratory Medicine, Okayama University Hospital, says, "Sar-j and isoQ reduced NNK-induced lung tumorigenesis. Sar-j targets both the initiation and growth or progression steps during carcinogenesis, specifically via anti-mutagenesis, stimulation of alkyl DNA adduct repair, and suppression of Akt-mediated growth signaling. IsoQ might contribute in part to the biological effects of sar-j via suppression of Akt phosphorylation, but it may not be the main active ingredient."

Their findings were published on December 9, 2022 in *Genes and Environment*.

In summary, the study shows that lung tumorigenesis in mice was suppressed following the oral intake of sar-j. Although [clinical trials](#) are warranted, the constituting components of sar-j, including isoQ, seem to be attractive candidates for chemoprevention.

More information: Jun Takata et al, Chemopreventive effects and anti-tumorigenic mechanisms of *Actinidia arguta*, known as sarunashi in Japan toward 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced lung tumorigenesis in a/J mouse, *Genes and Environment* (2022). DOI: [10.1186/s41021-022-00255-0](https://doi.org/10.1186/s41021-022-00255-0)

Provided by Okayama University

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