Annex A: Summary of Studies COT/2025/01

Extracts and concentrates of ginger

In this guide

Human Studies

Author/Date	Study type	Study size/No. of Patients at End	Exposure (ginger dose/day)	Study period	Length of Treatment (days)	Main outcome measures

Laekeman et al., 2021	Observational study, clinical feasability trial.	51/44	maximum of 2 tablets of 50 mg EXT.GR10 a day [limited data on actual amount administered]	During pregnancy.	NA	Patient satisfaction pregnancy complications (including hypertension and diabetes) and birth complications (including stillbirth, premature delivery, low birth weight).
Willetts *et al.,* 2003	Double-blind randomised placebo-controlled trial.	120/99	Ginger extract capsules (125 mg 4x/d =1000 mg/day).	8 months.	4	Used RINVR to measure frequency, duration, distress caused by nausea, vomiting and retching; long term follow-up for birth outcome.

Human studies – Platelet Aggregation

Author/date	Study design	Population/study size	Study Duration	Exposure	Outcome

Bordia *et al.,* 1997	NA	20	1 day. Outcomes measured at: baseline, 4 hours post-consumption.	10 g single dose. Unstandardised capsules.	Platelet aggregation Agonist(s): A and Epi.
Jiang *et al.,* 2004	Randomized, open label, three-way crossover trial.	Healthy male volunteers Age: 20–36 N =12.	Total study period: 3x13 days, 14 days washout period between each study period.	Dose: 3.6g (3x 0.4g, 3x per day) ginger extract Unstandardized capsules consumed with 25 mg dose of rac-warfarin, consumed once per study period.	Platelet aggregation Agonist: AA Plasma warf enantiomer protein binding & warfarin enantiomer concentrati Urinary S-7-hydroxywar

Rubin *et al.*, 2019	Case report	Female, 70 yrs	NA	48 mg daily Chewable ginger supplement for approx. 1 month.	INR - 8.0 ap 1 month aft taking ginge supplement
Verma *et al.,* 1993	Randomised placebo controlled trial.	Healthy male volunteers; N = 20.	Total study period: 14 days, high calorie diet for first 7 days, high-calorie diet and ginger/placebo consumed for next 7 days. Outcomes measured at baseline, 7, and 14 days.	Dose: 5g (4 x 625 mg, twice per day); dry ginger powder - Unstandardized capsules Consumed with 100g (2x50g) butter, 2 cups of milk, 8 slices of bread.	Platelet aggregation Agonist(s): A and Epi.

In vitro studies

Author	Test System	Exposure	Characterisation of test substance	Main outcome measure	Outc
Abudayyak *et al.,* 2015	Ames: Salmonella typhimurium TA98 and TA100 strains; Cytotoxicity assay: Rat kidney NRK-52E cell line.	Cytotoxicity assay: (0.75, 1.50, 3.00, 6.00, 12.00, 25.00, 50.00, and 75.00 mg/ml, genotoxicity: 0.78, 1.56, 3.13, 6.25, 12.50, and 25.00 mg/ml.	Aq, chloroform and MeOH ginger extracts.	Cytotoxicity and genotoxicity.	Chlor extra cytot = 9.0 aque muta conc agair strai prese mix.
Mohammed *et al.,* 2016	chick embryonic heart micromass; mouse D3 embryonic stem cell systems (ESD3).	0.75–100 uM Micromass assay: 6 days, ESD3: 12 days.	6-gingerol	Embryotoxicity	no si chan contr cellu or ch total conte ginge prim embr cardi
NA	NA	NA	NA	NA	Inhib contr activ 12.5-

NA	NA	NA	NA	NA	Char cellu and conte dose mann conc µg/m
NA	NA	NA	NA	NA	Signi decr cardi diffe for a conc exce µg/m
NA	NA	NA	NA	NA	Signi decr cellu and conte cell-c cardi with 6-gin conc expo
Nakamura & Yamamoto (1982)	Escherichia coli Hs30.	Not specified.	Juice of ginger rhizome, 6-gingerol.	Mutagenicity	ginge supr spon muta ginge muta isola

Nakamura & Yamamoto 1983	Escherichia coli Hs30.	Not specified.	6-shogaol, 6-gingerol.	Mutagenicity.	[6]-S 10^4 t mut conc 700u [6]-g
Nirmala *et al.,* 2007	Wistar rats, male	Salmonella typhimurium strains TA 98 and TA 100.	Ginger paste and powder, unboiled, boiled, unfried, fried. Ames test: Ginger paste: 1, 2 and 3 mg; powder: 0.5, 1 and 1.5 g.	Anti-mutagenicity.	Anti- poter unalt treat ginge
Plengsuriyakarn *et al.,* 2012	Cholangiocarcinoma (CCA) cell line 6 (CL-6), hepatocarcinoma (HepG2) and normal human renal epithelium (HRE).	1.95, 3.90, 7.81, 15.62, 31.25, 62.5, 125, and 250 µg/ml.	Crude ethanolic ginger extract.	Cytotoxicity	IC50 cytot 10.9 µg/m
Soudamini *et al.,* 1995	Salmonella typhimurium strains TA 100, 98 and TA 1535.	25 and 50 mg/plate.	ethanolic mixture of powdered ginger.	Mutagenicity	muta both and T both conc
Zaeoung *et al.,* 2005	breast (MCF7) and colon (LS174T) cell lines.	Not specified.	aqueous extract and volatile oils.	Cytotoxicity	IC50 µg/m

In vivo studies

Author	Test System	Study size	Exposure	Characterisation of test substance	Duration
Alnaqeeb *et al.,* 2003 (abstract)	Rats, female	Unknown	Oral and intraperitoneal. 50 mg/kg and 500 mg/kg	Aqueous ginger extract	28 days
Dissabandara & Chandrasekara, 2007	Sprague-Dawley rats.	15 in 3 groups, otherwise not specified.	Oral: 500 mg/kg/day and 1000 mg/kg/day during days 5 to 15 of gestation.	Powdered ginger extract.	Animals treated with ginger for 10 days.

ElMazoudy and Attia, 2018 (abstract only)	ICR mice	Unknown	250, 500, 1000, or 2000 mg/kg bw/d aqueous ginger extract.	Powdered dried ginger root	35-day treatment study; 20 day study (antifertility and abortifacien loss).
Hosseini *et al.,* 2015 (abstract only)	Rats, female and male offspring	72 (groups of 9)	Oral: 50, 100 and 200 mg/kg bw during neonatal and perinatal periods.	Alcoholic ginger extract	Unknown

Jeena *et al.*, 2011	Wistar rat	30	Oral: 100, 250, and 500 mg/kg per day once daily.	Ginger essential oil.	13 weeks.
Malik and Sharma, 2011	Wistar rat, male.	Not specified.	gastric gavage: 250, 500 and 1000 mg/kg, (corresponding to 5, 10 and 20% of the NOAEL of the lyophilised ginger powder (5000 mg/kg).	Lyophilsed ginger juice powder.	Experiment 2: 8 weeks. Exp 1&2 no specified.

Peneme et al., 2023	Swiss mice.	6	5000 mg/kg aqueous ginger extract.	Ginger powder extracted into water.	OECD guideline no. 423.
NA	NA	20	17 β-oestradiol, (1 mg/kg) or ginger extract (300 or 600 mg/kg) per day.	Ginger powder extracted into water.	2 weeks.
Plengsuriyakarn *et al.,* 2012	OV and nitrosamine (OV/ DMN)-induced CCA hamsters.	90	1000, 3000, and 5000 mg/kg bw/d.	NA	30 days
Rong *et al.*, 2009.	Sprague–Dawley rats, male and Female.	40.	Gavage: 500, 1000 and 2000 mg/kg bw/day.	Powdered Japanese ginger.	37

Shalaby and Hamowieh, 2010	Sprague Dawley rats.	120	Oral, 5 to 17.5 g/kg bw.	Water or methanolic ginger extract.	65 days.
NA	NA	NA	NA	NA	NA

NA	NA	NA	100 and 200 mg/kg bw for 65 days and water extracts at doses of 150 and 300 mg/kg bw.	NA	NA
Weidner & Sigwart, 2001	Wistar rats, pregnant female.	176 (88 Females).	Gastric intubation: 100, 333 and 1000 mg/kg from days 6-15.	EV.EXT 33, a patented Zingiber officinale extract (comprising 6-gingerol, 8-gingerol, 10-gingerol, 6-shogaol, and 8-shogaol (1.9 w/w of the extract).	21 days.