

Deoxynivalenol- past, present, future

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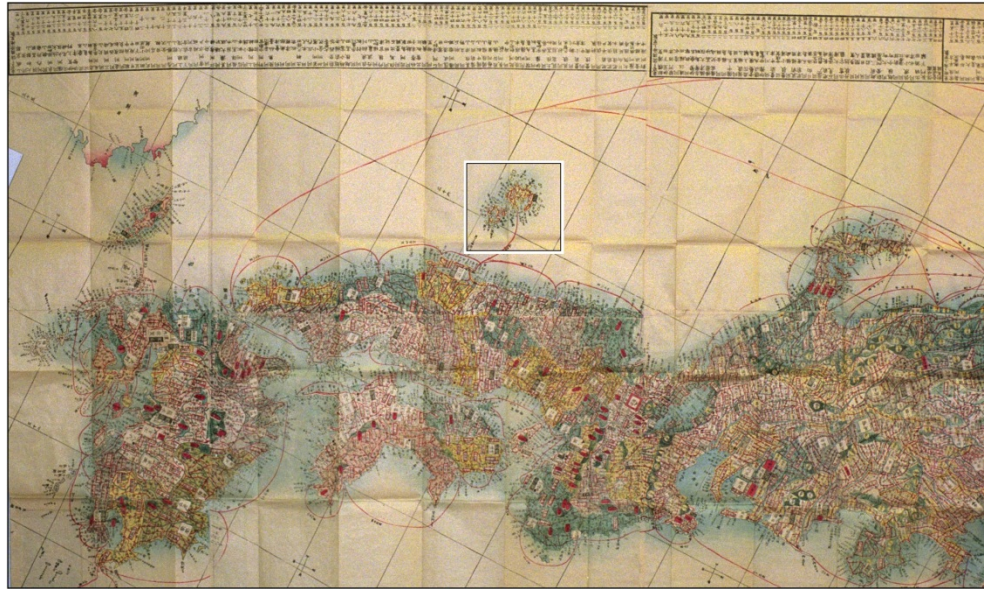




Spanish cultivars were brought to Florida during the 15th century which spread south. Early colonists brought cultivars from their homes throughout the UK and Europe. By 1721 a 20000 ton crop was produced. In the 13 Colonies, the conditions were more suitable for maize. In Quebec and Connecticut scab was a problem in the late 17th century. Animal toxicoses were known by the 1880s.

Fusarium Head Blight was known to be associated with climate by the 1880s and systematic disease reports began ca. 1900 in the US and Canada.

1880 Japan



Wheat was grown in the far east before Marco Polo made it to China. “Red mold poisoning” (*Akakabi-byo*) was reported in rural Japan coincident with an increase in wheat production from 1800. The fungus was reported as *F. graminearum* by 1912. Major epidemics were recorded in Japan for the 1890, 1901, 1914, 1932, 1946, 1958, 1963 and 1970 crops, with human and animal toxicoses reported throughout this period. The primary literature is in Japanese.

Mycotoxins (1974): 263; Dev Food Sci 44:195; Asian Med J 31:599

China 1961-1987 incidents of FHB-associated toxicosis involving 8000 people reported by Min Public Health; “nausea, abdominal pain, diarrhea, dizziness and headaches, sometimes after an interval”. Samples from the late 1980s cases contained >10 ppm DON. The primary literature is in Chinese.

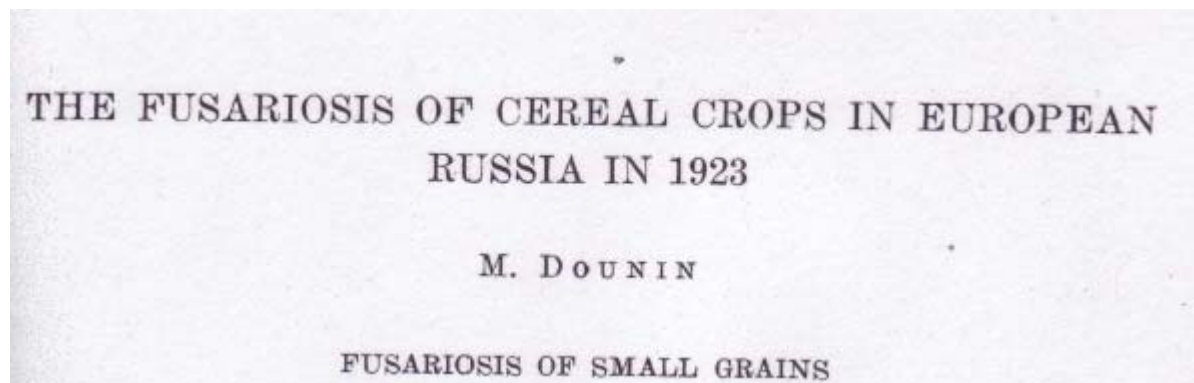
Mycotoxins in Grain 1994; 509; Mycotox Res 10:21



The summer of 1923 was extraordinarily rainy and it had many cloudy days. This probably accounts for the widespread prevalence of the genus *Fusarium* Link on the cereal crops of Russia.

In connection with the extraordinary prevalence of *Fusarium roseum* Lk. on cereals, it was observed that the bread became poisonous (inebriant bread). People who ate it suffered from weakness vertigo, headache, nausea and vomition”

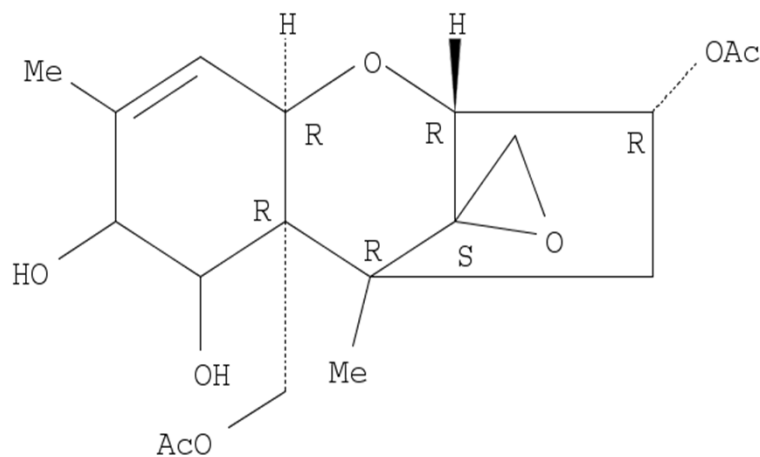
Phytopathology 1926 16:305

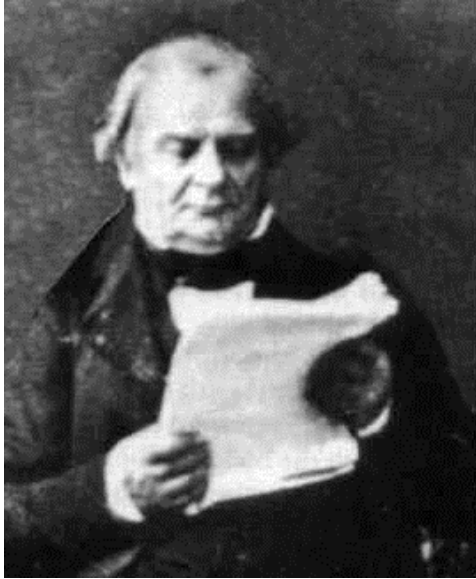


In 1928, there was a massive epidemic in the mid west. Some of this grain was exported to Germany where the resulting feed caused wide-spread poisoning of swine.

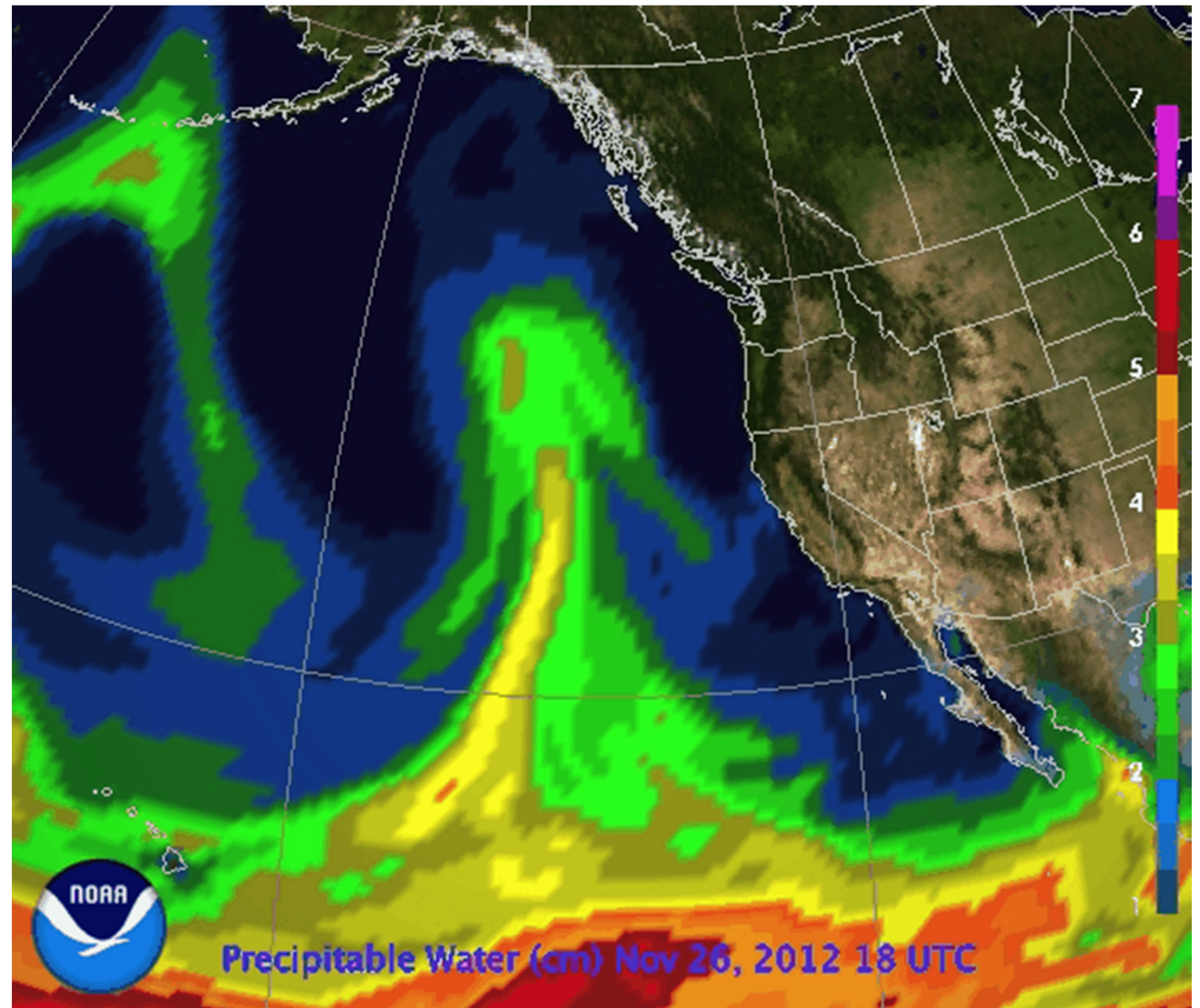
Similar effects were reported in the US. Scientists showed that damaged barley resulted in emesis in swine. By 1941, a water extract of barley contaminated by a fungus described as *G. saubentii* [an invalid name that included *F. graminearum*], induced emesis in swine by gavage. Both German and US scientists pursued the identity of the toxin variously thought to be a protein, choline or fatty acid esters of choline, glucosides or basic nitrogen compounds or an alkaloid.

The investigation was continued by some of the same ARS researchers who started in the 1930s until the late 1960s. Some Australian researchers independently reported an emetic principle from *F. culmorum* & *F. graminearum* damaged corn in 1967.





$$H_{TS} = H_R \exp\left[\frac{-\Delta H_{v,TS}}{R_C}\left(\frac{1}{T_S} - \frac{1}{T_R}\right)\right]$$



Current TDI

belongs to the B group of trichothecenes. In 1980, there was very little relevant toxicological information available on DON. As pure DON became available, this situation has improved. Biochemically, trichothecenes, including DON, are inhibitors of protein and DNA synthesis. So far, only negative results have been obtained in mutagenicity tests (Rogers and Héroux-Metcalf 1983). Short-term effects of oral intake of DON by rodents (gavage, diet), as well as effects on reproduction, including teratogenic potential, were assessed at the Health Protection Branch (Khera et al. 1982, 1984). These studies have shown a preliminary no effect level (NOEL) of $0.75 \text{ mg.kg b.w.}^{-1}$. At higher dosage levels, reproductive, embryotoxic, and possible teratogenic effects were noted. Deoxynivalenol also affected food intake, body weight and the immune system. Further studies in rodents

→ Based on the toxicity information on DON available early in 1983 a tentative tolerable daily intake of $3.0 \text{ } \mu\text{g.kg b.w.}^{-1}$ for adults and $1.5 \text{ } \mu\text{g.kg b.w.}^{-1}$ for infants was established.

Preliminary guideline levels of DON were therefore adjusted upwards in 1982 to $2.0 \text{ } \mu\text{g.g}^{-1}$ from $0.6 \text{ } \mu\text{g.g}^{-1}$ in uncleaned soft wheat used for non-staple foods including bran, except for soft wheat destined for infant food where the guideline level is $1.0 \text{ } \mu\text{g.g}^{-1}$. As a result of processing, levels of $1.2 \text{ } \mu\text{g.g}^{-1}$ and $0.6 \text{ } \mu\text{g.g}^{-1}$ DON would be expected in the flour portion of finished foods and infant foods respectively.

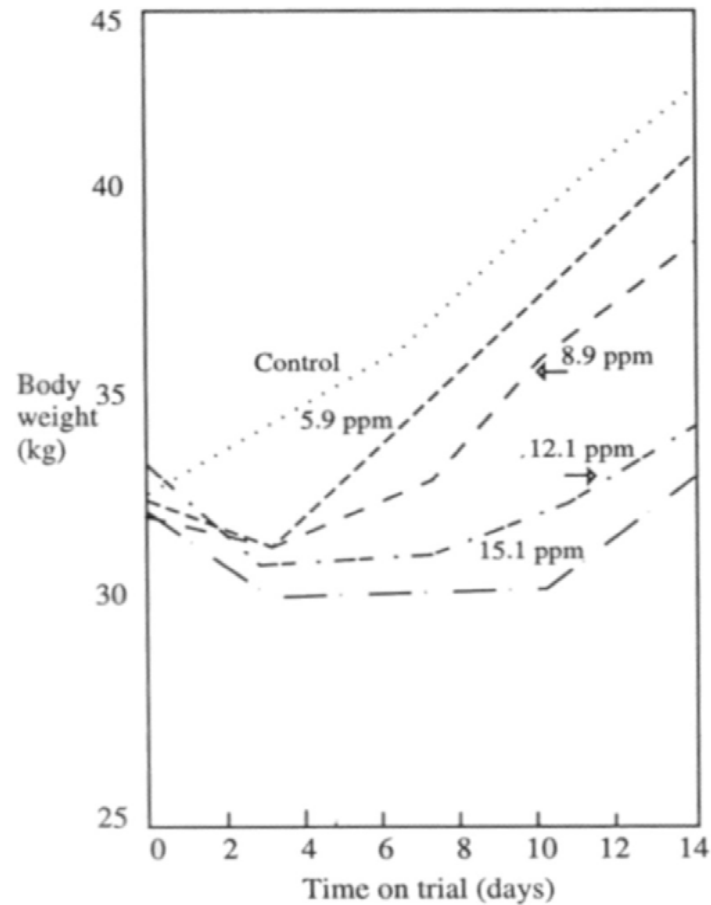
Mycotoxins: a Canadian perspective.

Scott PM, Trenholm HL, Sutton MD (1985)

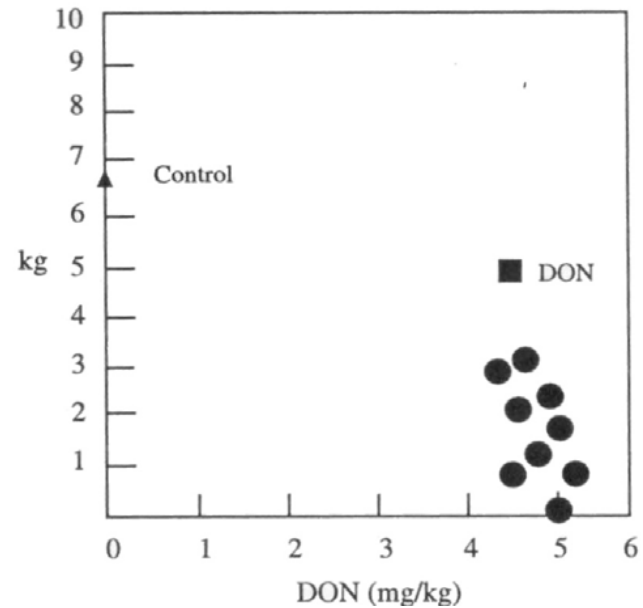
National Research Council Canada 22848, p. 109-110

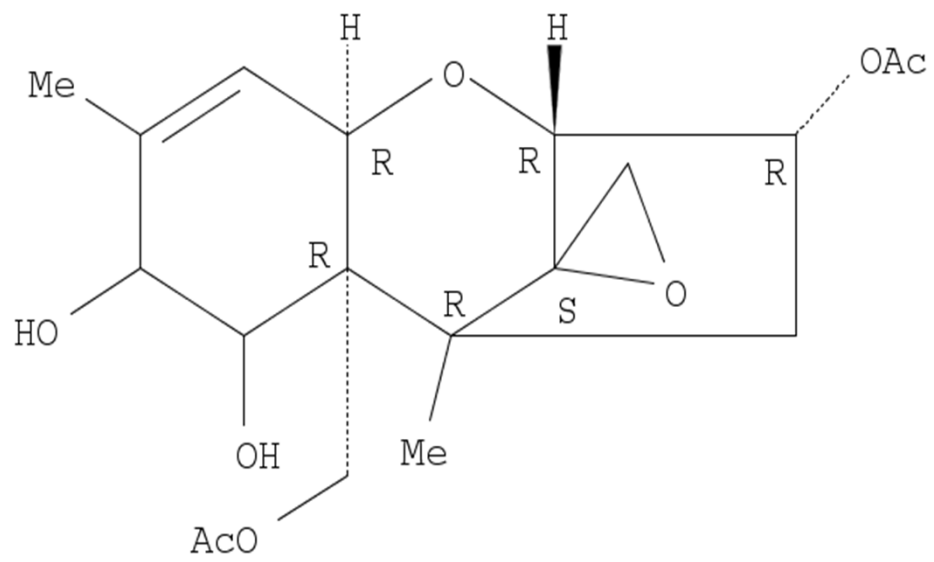
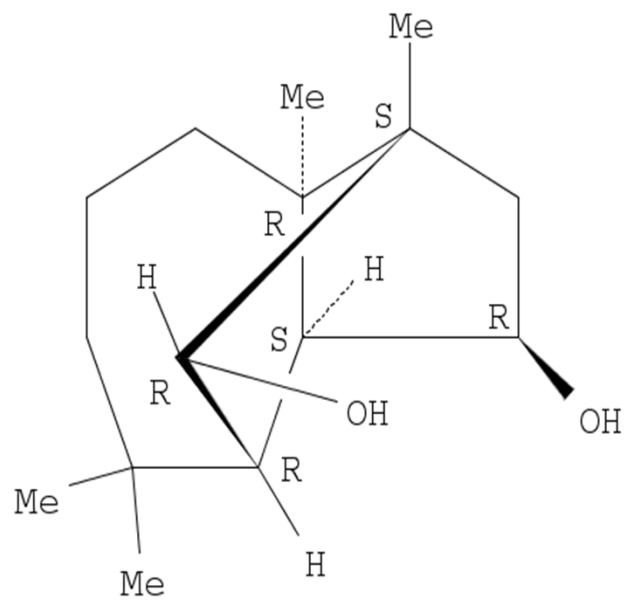
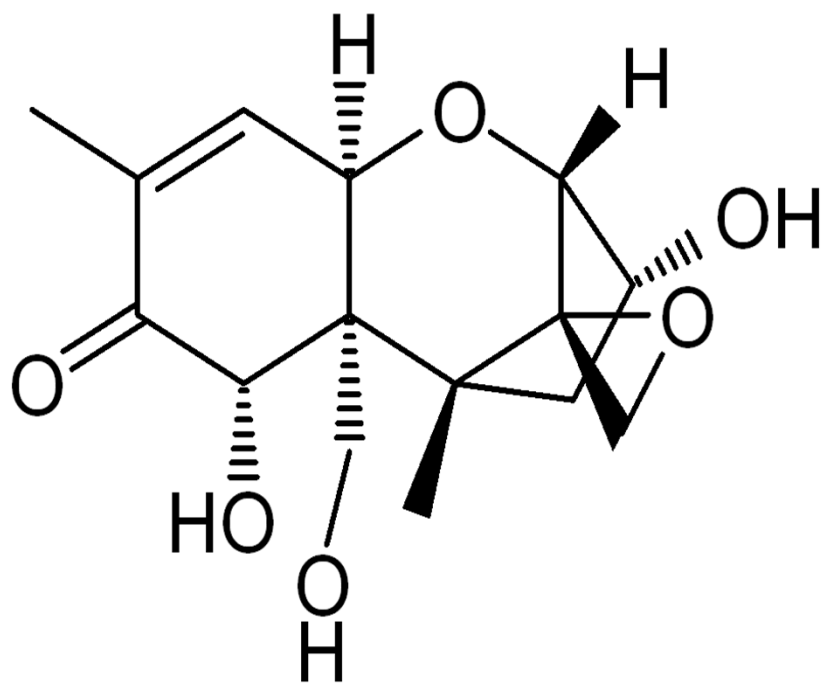


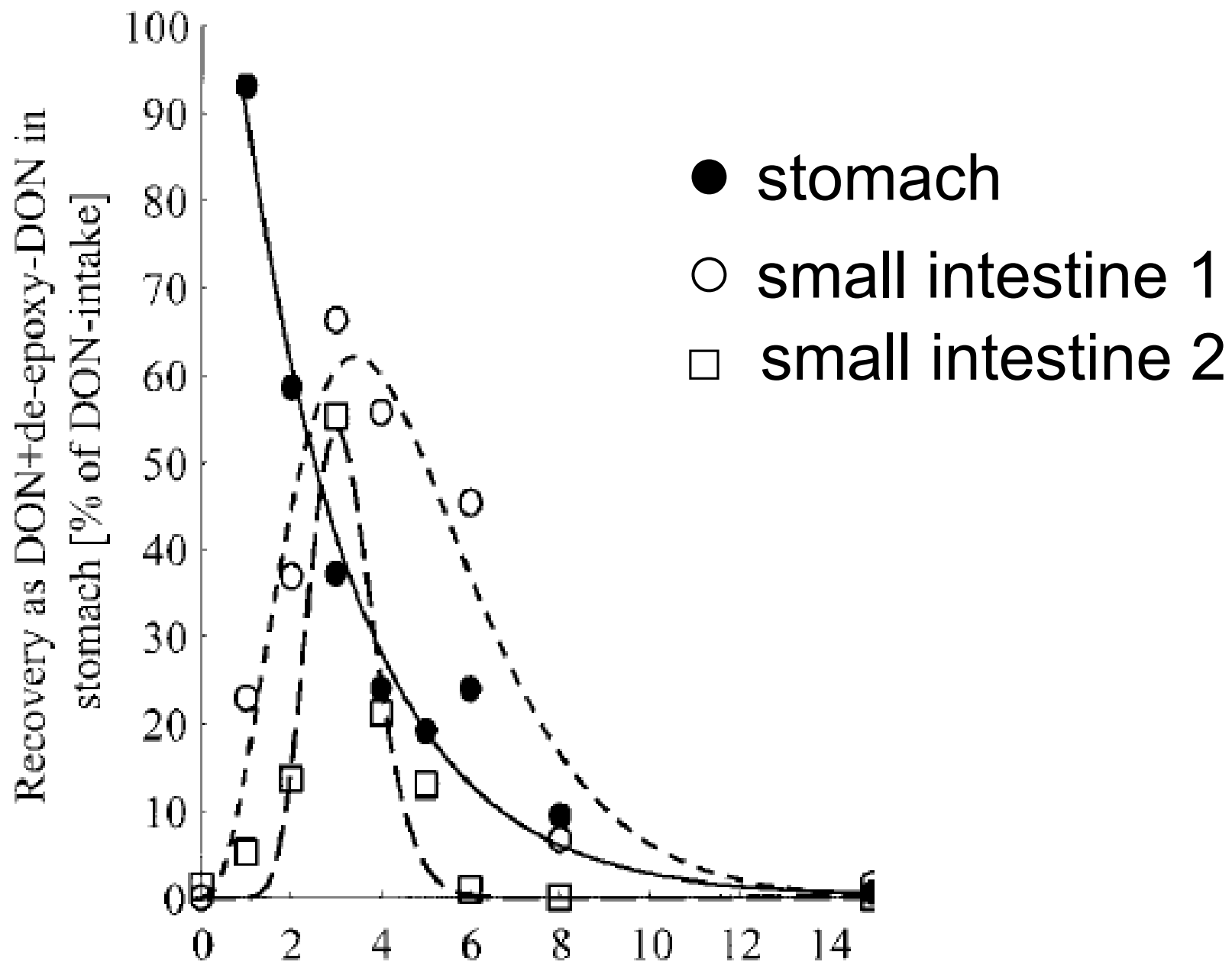
Effect of pure DON on growth of swine



Effect of grain naturally contaminated with DON on growth of pigs







	ng of DON/g of tissue ^b ± SD					<i>t</i> _{1/2} , ^c h
	0.33 h	1 h	3 h	8 h	24 h	
plasma	1337.3 ± 84.2	1044.3 ± 303.9	551.3 ± 161.6	155.5 ± 86.1	17.8 ± 6.6	3.90
kidney	1675.8 ± 391.9	1985.3 ± 725.2	930.5 ± 363.1	330.8 ± 160.7	10.0 ± 4.2	3.15
liver	1114.3 ± 153.9	735.3 ± 219.0	439.3 ± 99.2	207.3 ± 79.7	8.2 ± 5.5	3.48
abdominal fat	419.7 ± 127.1	491.6 ± 146.6	327.1 ± 228.7	78.0 ± 49.8	3.4 ± 3.4	3.30
back fat	224.7 ± 79.5	294.7 ± 95.9	133.7 ± 28.0	86.6 ± 24.2	12.4 ± 5.1	5.50
lymph	273.6 ± 142.8	292.3 ± 59.7	141.4 ± 80.9	48.7 ± 31.2	0.8 ± 1.0	2.77
lung	265.9 ± 58.7	203.2 ± 55.1	77.5 ± 14.5	35.3 ± 8.5	1.0 ± 1.2	3.04
adrenals	242.2 ± 142.0	237.0 ± 111.5	68.9 ± 67.2	22.1 ± 21.7	nd ^c	1.82
spleen	165.0 ± 32.6	148.9 ± 42.4	73.8 ± 26.2	9.6 ± 3.3	nd	1.82
testes	121.3 ± 33.8	123.8 ± 43.8	54.4 ± 16.2	15.2 ± 4.8	nd	2.47
brain ←	54.9 ± 17.3	51.5 ± 18.6	28.9 ± 7.3	15.6 ± 6.6	nd	4.70
heart	31.4 ± 10.6	48.0 ± 22.8	11.1 ± 4.9	2.0 ± 0.8	nd	1.75
muscle	32.1 ± 11.7	33.1 ± 8.5	19.1 ± 3.0	4.6 ± 2.4	nd	2.62
skin	31.0 ± 20.6	28.8 ± 13.5	16.1 ± 8.7	4.9 ± 3.4	nd	2.83
intestine	20.4 ± 5.8	17.5 ± 6.0	5.1 ± 3.8	1.6 ± 2.1	nd	2.07
pancreas	17.6 ± 8.0	18.7 ± 17.5	4.0 ± 2.6	nd	nd	1.16
urine	87892.5 ± 23311.4	139885.0 ± 136966.1	45750.0 ± 38993.5	15740.0 ± 12840.7	477.5 ± 510.6	
bile	1900.0 ± 589.7	5480.0 ± 2957.2	10935.0 ± 369.6	10962.5 ± 5527.8	1283.0 ± 678.5	

Doc Pestka's diet pills: not all drugs are as well studied!

many changes now documented

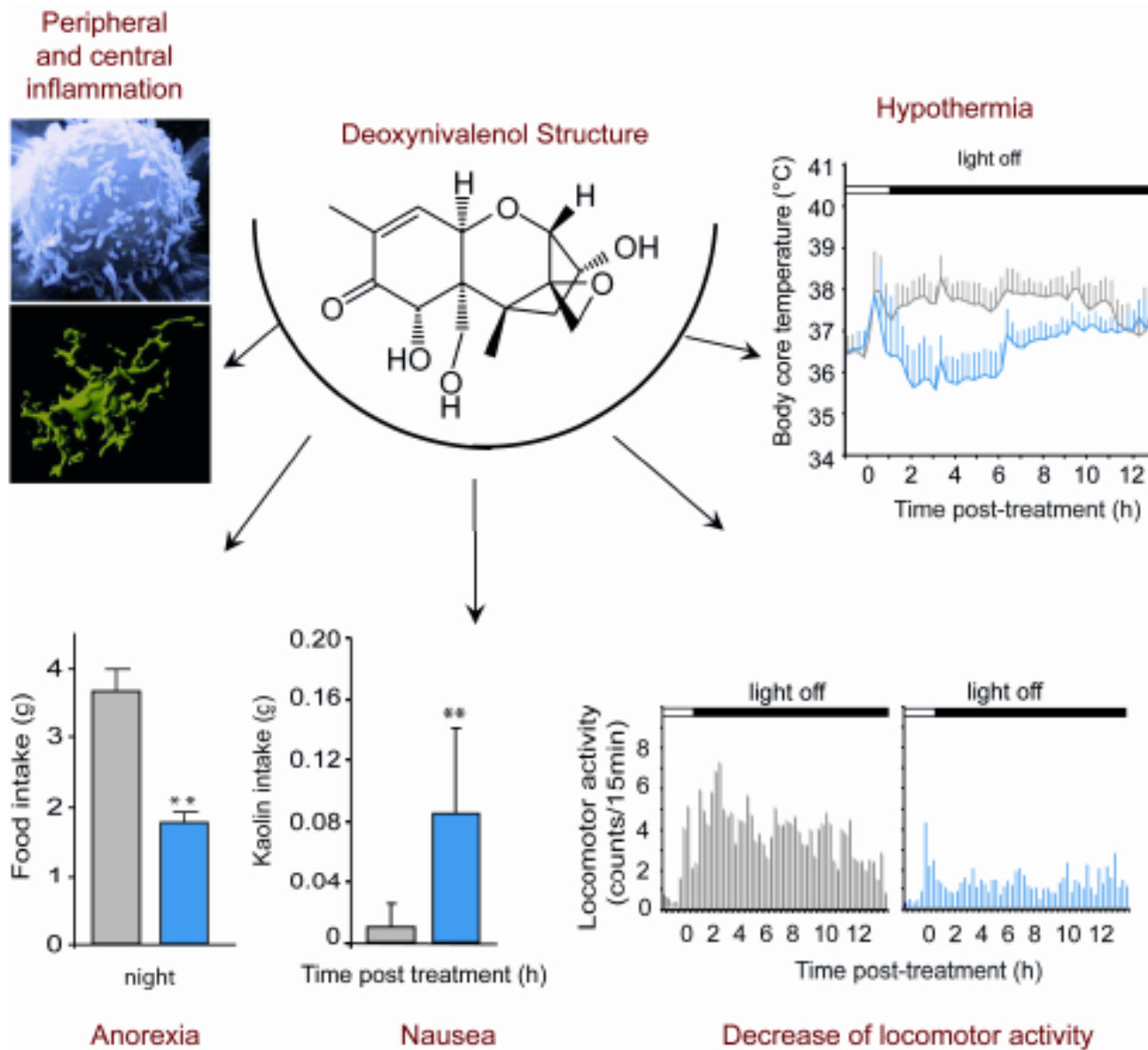
in the brain →

in blood cells



gut satiety hormone peptide YY →

in gut cell immune response



hypothalamus frontal cortex cerebellum

norepinephrine

↑

↑

↑

dopamine

↓

↓

↓

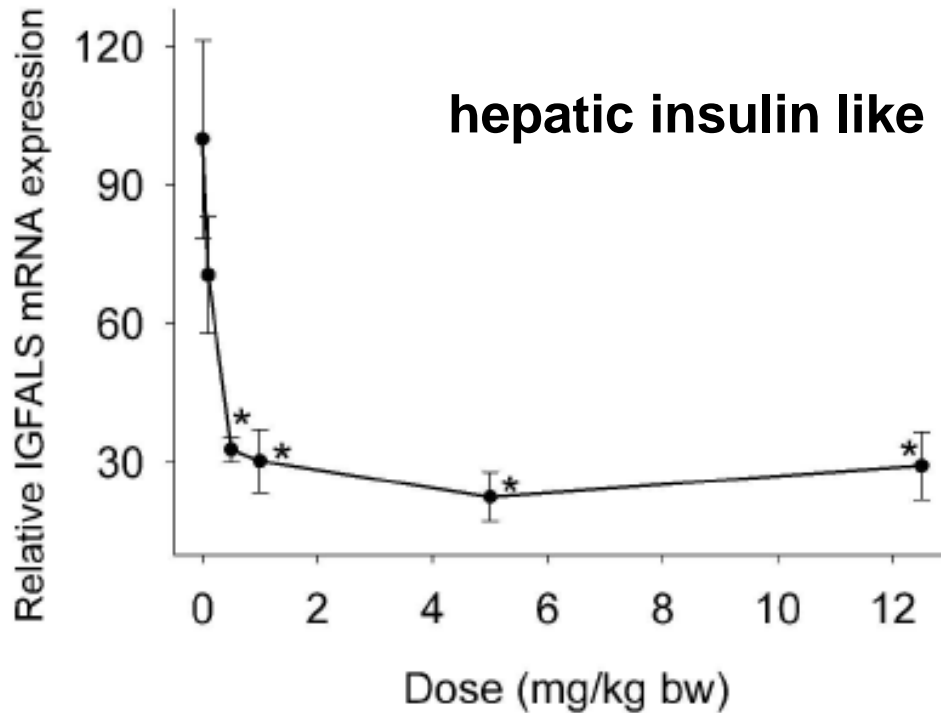
serotonin

↑ then ↓

↓

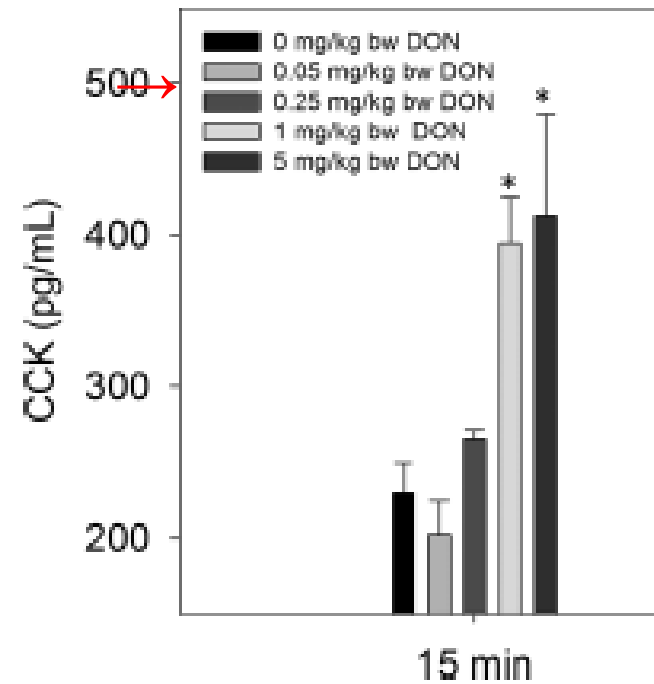
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J Environ Science & Health (1994) B29:1203



Gut Satiety Hormone Peptide YY

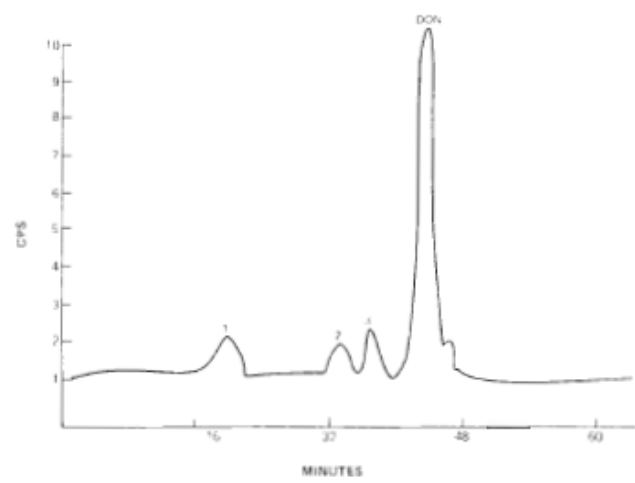
i.p.



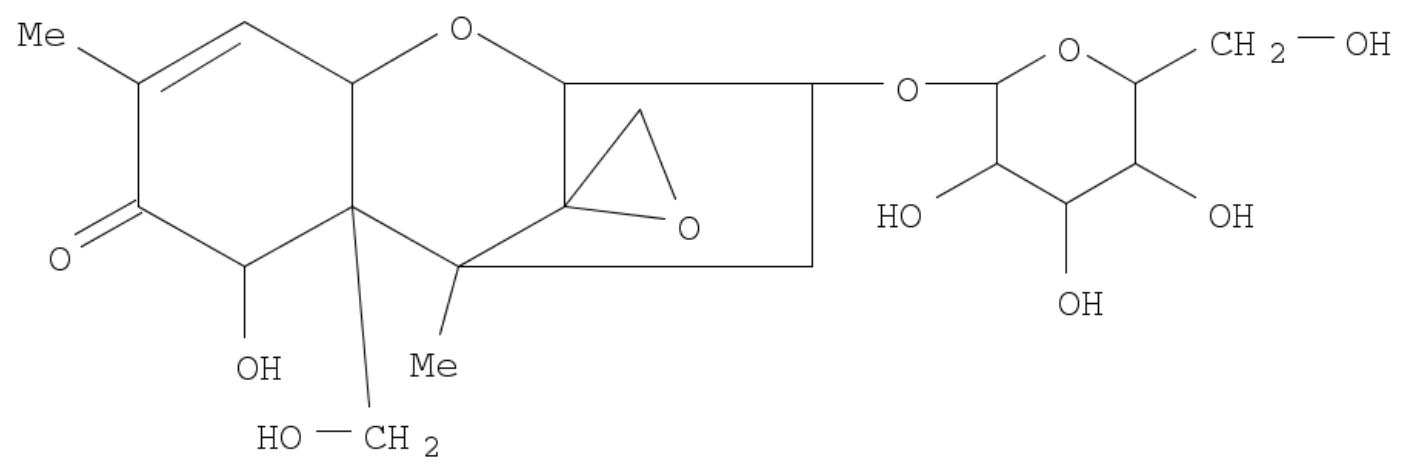
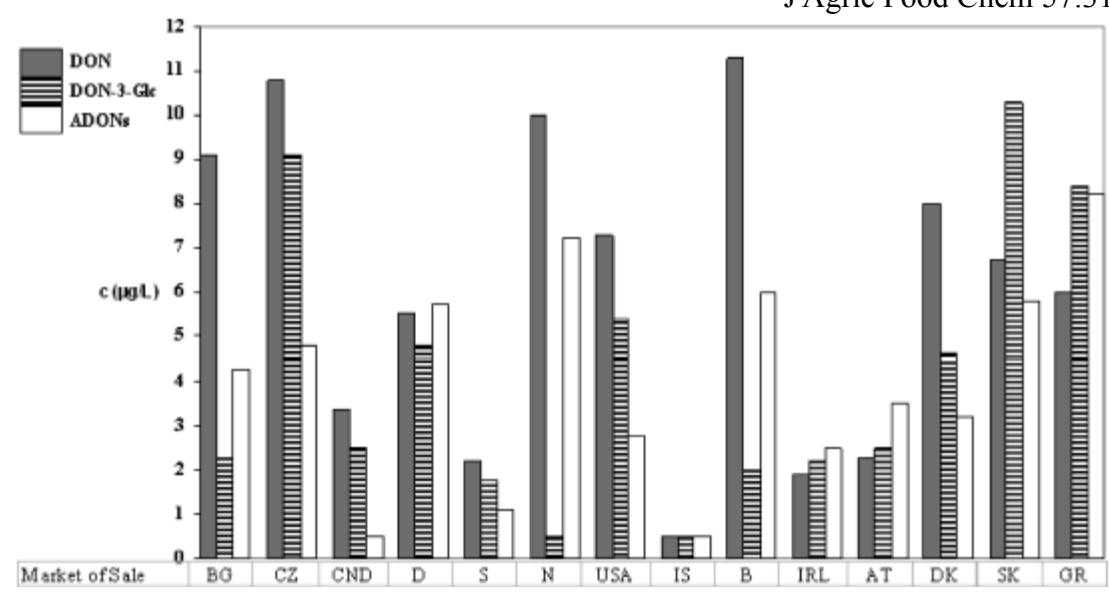
Comparison of Effects of Orolingual and ip Exposure to DON on Food Intake and Gut Satiety Hormone Release

oral

Endpoint	Orolingual exposure		ip exposure	
	Vehicle	DON	Vehicle	DON
Food intake over 2 h (g)	0.87 ± 0.26	0.29 ± 0.05*	0.76 ± 0.05*	0.24 ± 0.05**
PYY (pg/ml)	108 ± 15.1	229 ± 25.3*	105 ± 17.5	276 ± 55.9*
CCK (pg/ml)	260 ± 41.4	741 ± 41.6*	303 ± 24.3	753 ± 21.5*



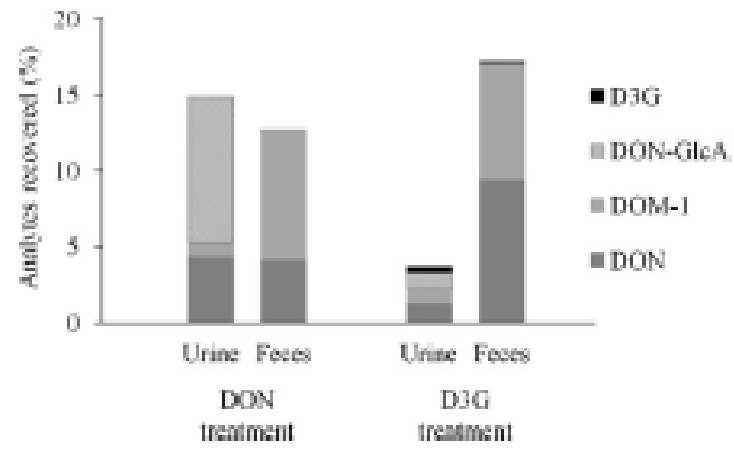
Can J Plant Pathology 8:147



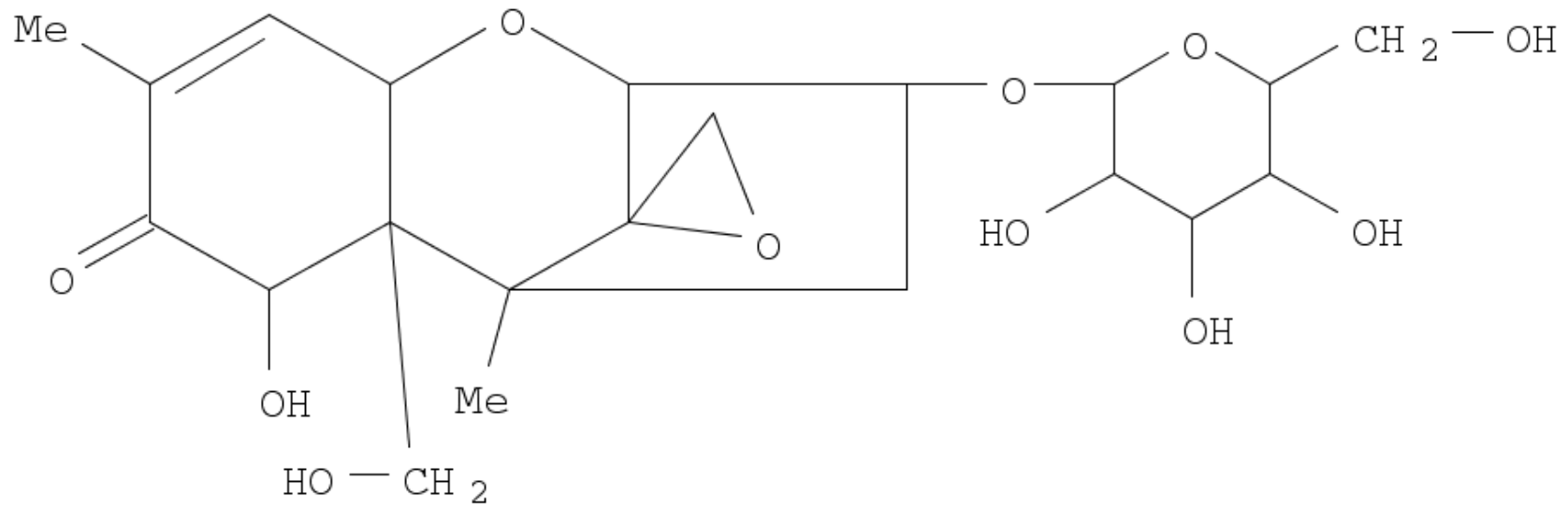
Wheat cultivar	Harvest year	DON ($\mu\text{g}/\text{kg}$)	DON-3-glucoside ($\mu\text{g}/\text{kg}$)	Percentage (%) (DON-3-glucoside/DON \times 100)
Abika	2006	2,903	310	11
Abika	2007	7,097	590	8.3
Alchemy	2006	2,372	230	9.7
Ambition	2006	3,936	506	13
Tommi	2006	3,778	421	11
Glasgow	2006	5,427	327	6.0
Glasgow	2007	7,258	1,020	14
Naturastar	2006	3,325	414	13
Naturastar	2007	3,751	640	17
Penta	2006	2,023	297	15
Ritmo	2006	4,270	694	16
Robigus	2006	3,377	679	20
Robigus	2007	9,479	1,353	14
Skalmeje	2006	2,698	424	16
Smuggler	2006	3,570	583	16
Smuggler	2007	6,871	1,205	18
Terra	2006	1,955	346	18
Olivin	2006	788	39	4.9
Olivin	2007	5,218	563	11
Hanseat	2006	4,322	1,038	24
Hanseat	2007	6,139	652	11

µg/kg toxin

	Fibre-enriched bread	Bran-enriched bread	Cornflakes	Popcorn	Oatmeal	Fibre-enriched bread	Bran-enriched bread	Cornflakes	Popcorn	Oatmeal
DON ²	15 ^a	17 ^a	28 ^a	3 ^a	10 ^a	43 ^b	31 ^a	53 ^a	72 ^{ab}	30 ^{ab}
3-ADON	23 ^a	32 ^a	36 ^a	32 ^a	74 ^b	10 ^a	3 ^a	29 ^a	30 ^b	nd ^{ab}
15-ADON	5 ^a	6 ^a	18 ^a	10 ^a	11 ^a	11 ^a	8 ^a	6 ^a	34 ^b	2 ^{ab}
DON-3G	15 ^a	17 ^a	26 ^a	21 ^a	41 ^a	43 ^a	25 ^a	7 ^a	40 ^{ab}	7 ^a
ZEA	17 ^a	40 ^a	72 ^a	15 ^a	32 ^a	34 ^a	37 ^a	78 ^a	6 ^a	57 ^a
ZEA-4G	1 ^a	6 ^a	2 ^a	nd ^a	3 ^a	21 ^a	28 ^{ab}	59 ^b	nd ^a	25 ^{ab}
ZEA-4S	1 ^a	nd ^a	nd ^a	nd ^a	2 ^a	5 ^a	8 ^a	35 ^b	2 ^a	7 ^a
α-ZOL	12 ^a	10 ^a	2 ^a	1 ^a	17 ^a	3 ^a	2 ^a	54 ^b	4 ^a	nd ^a
α-ZOL-4G	nd ^a	1 ^a	nd ^a	nd ^a	1 ^a	4 ^a	nd ^a	16 ^a	nd ^b	nd ^b
β-ZOL	18 ^a	19 ^a	16 ^a	14 ^a	13 ^a	2 ^a	8 ^{ab}	17 ^b	nd ^a	nd ^a
β-ZOL-4G	nd ^a	2 ^a	nd ^a	nd ^a	1 ^a	10 ^a	10 ^a	17 ^a	1 ^a	2 ^a
Total DON derivatives (%) ³	62 ^{ab}	70 ^{ab}	68 ^{ab}	96 ^{bc}	95 ^c	36 ^a	40 ^a	33 ^a	75 ^a	9 ^a
3-ADON and 15-ADON (%)	41 ^a	49 ^a	45 ^a	64 ^a	70 ^a	14 ^a	19 ^a	25 ^a	45 ^b	2 ^a
DON-3G (%)	22 ^a	21 ^a	23 ^a	31 ^a	26 ^a	22 ^a	21 ^a	8 ^a	30 ^a	6 ^a
Total ZEA derivatives (%)	43 ^a	36 ^a	45 ^a	29 ^a	39 ^a	42 ^a	58 ^a	68 ^a	25 ^a	41 ^a
ZEA-4G, α-ZOL-4G and β-ZOL-4G (%)	4 ^a	6 ^a	1 ^a	nd ^a	7 ^a	36 ^a	39 ^a	35 ^a	6 ^a	10 ^a



Toxicology Letters 213:367

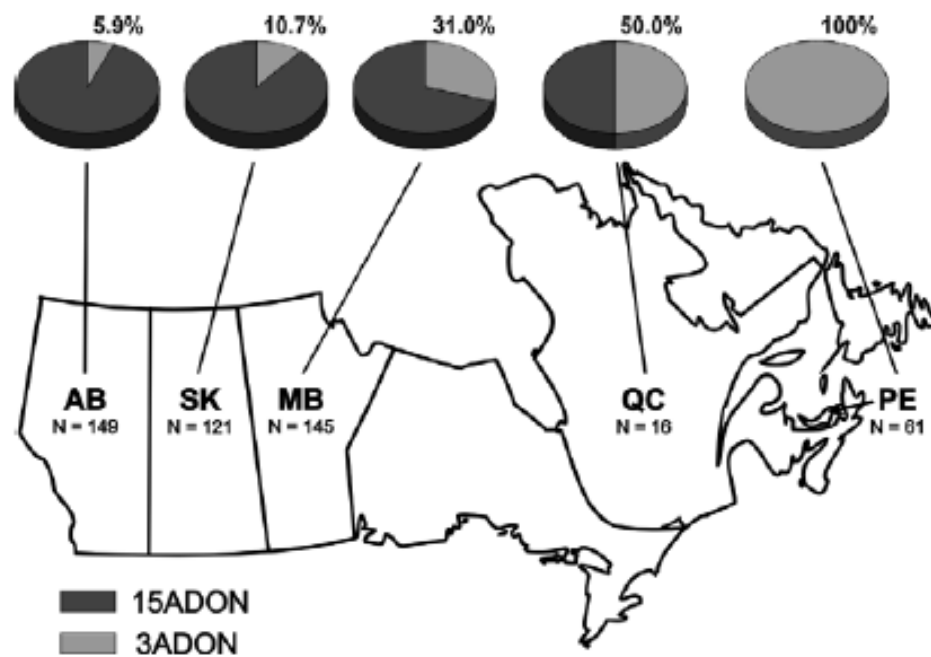


Comparison of Effects of Orolingual and ip Exposure to DON on Food Intake and Gut Satiety Hormone Release

Endpoint	Orolingual exposure		ip exposure	
	Vehicle	DON	Vehicle	DON
Food intake over 2 h (g)	0.87 ± 0.26	0.29 ± 0.05*	0.76 ± 0.05 ^a	0.24 ± 0.05 ^{*a}
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	DON ($\mu\text{g/L}$)	15-A-DON ($\mu\text{g/L}$)
<i>F. graminearum</i>		
DAOM 178151 (Canada)	—	—
177408	—	—
177406	1430	522
180376	1490	2725
180377	166	2850
180378	181	441
180379	359	1660 ^g
177409	11	1340 ^g
177410	—	333
178148	496	13700
178149	148	140
178150	173	121
M 69 ^b	2470	29600
B 425 ^c (U.S.A.)	310	3380
B 426	432	2410
B 350	—	—
B 352	—	—
M 74 (Canada)	299	3660
M 309	316	381
HLX 1501		+
NRRL 5883 (U.S.A.)		+
<i>F. roseum</i> ATCC 28114 ^d	432	13700 ^g

Can J Microbiol 29: 1171

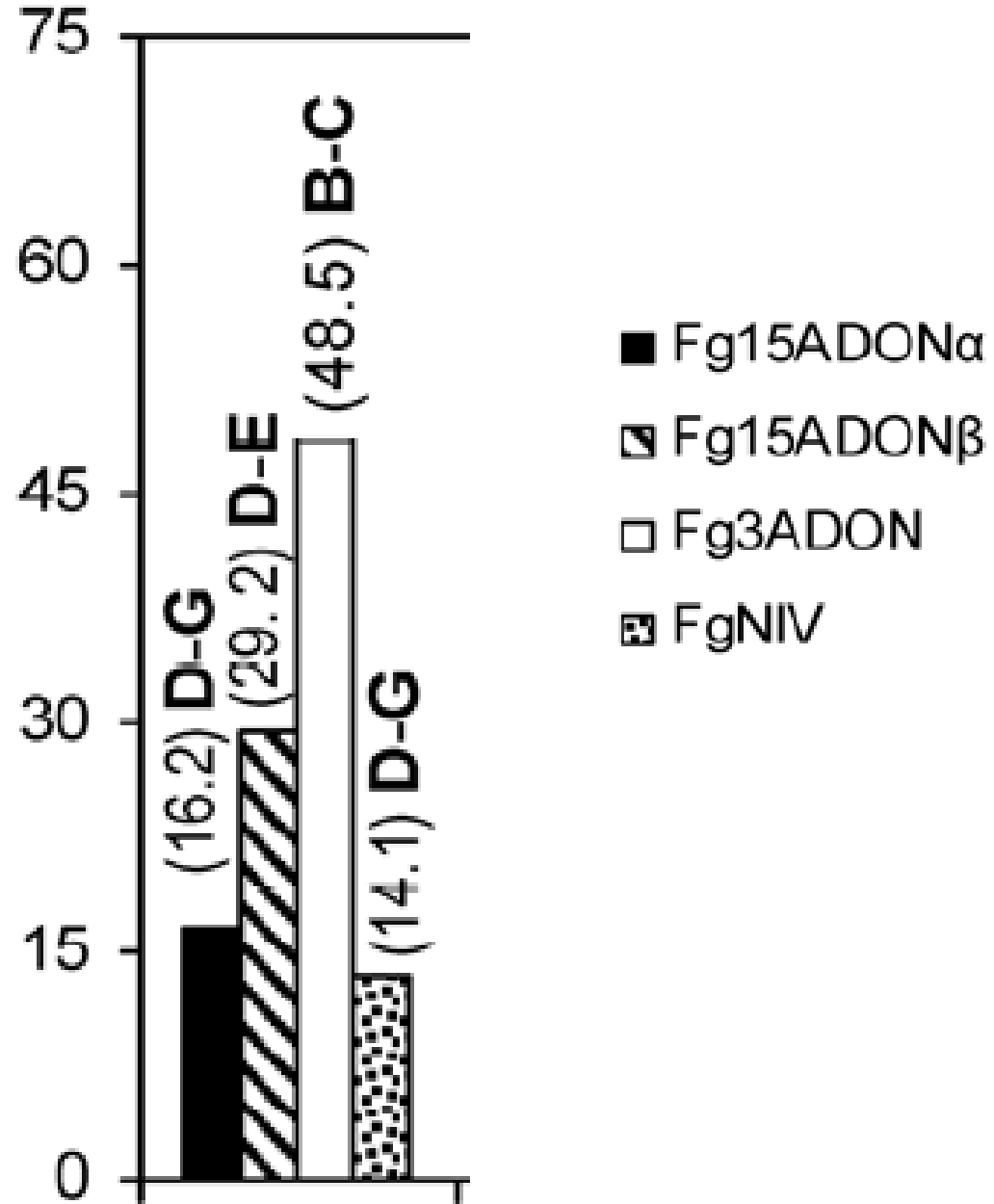


Cultivar	Chemotype ^a	FHB severity ^b 14 dai ^c	FHB severity 21 dai
5602 HR	3-ADON	45.7 ^d	72.0
	15-ADON	50.0	76.7
Roblin	3-ADON	57.7	85.3
	15-ADON	56.7	83.3

DON ppm All isolates

Province	5602HR	Roblin
Alberta	14.3 ^a	23.8 b
Saskatchewan	15.1	30.5 a
Manitoba	13.3	33.3 a

Chemotype	DON ppm	ADON ppm	DON ppm	ADON ppm
3-ADON	16.1	0.54	32.6 a	0.80 b
15-ADON	12.5	0.82	25.8 b	1.42 a



As 3-acetyl-deoxynivalenol (3-Ac-DON) is converted to deoxynivalenol (DON) in vivo and therefore contributes to the total DON-induced toxicity, the Committee decided to convert the provisional maximum tolerable daily intake (PMTDI) for DON to a group PMTDI of 1 µg/kg bw for DON and its acetylated derivatives (3-Ac-DON and 15-Ac-DON). In this regard, the Committee considered the toxicity of the acetylated derivatives equal to that of DON. The Committee concluded that, at this time, there was insufficient information to include DON-3-glucoside in the group PMTDI.



Food and Agriculture Organization
of the United Nations



World Health
Organization

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
Seventy-second meeting
Rome, 16–25 February 2010

SUMMARY AND CONCLUSIONS
Issued 16th March 2010

IMPLICATIONS OF GLOBAL CLIMATE CHANGE FOR THE
ASSESSMENT AND MANAGEMENT OF HUMAN HEALTH RISKS OF
CHEMICALS IN THE NATURAL ENVIRONMENT

JOHN M. BALBUS, *† ALISTAIR B.A. BOXALL, ‡ RICHARD A. FENSKE, § THOMAS E. MCKONE, || and
LAUREN ZEISE #

“Increases in risks are likely to be seen for the natural toxins that are produced by microbes, algae, and plants. These alterations in risks have implications for national and international decision makers involved in the ... monitoring and management of chemicals in environmental matrices and foodstuffs. The expected changes reveal that some of the scenarios and models currently used in health risk assessment of chemicals will need updates and revision in order to reflect future changes.”



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“Monitoring methodologies may also need to be adapted in order to cope with increased variability in exposure, sensitivity, and risk, both spatially and temporally. Monitoring and sampling should be done at a frequency sufficient to capture variability, which is likely to increase in many places”

