Carbamazepine in biosolids amended soils- Environmental Implications

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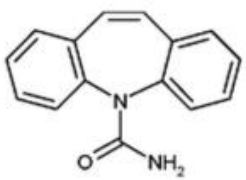
Why we are concerned: Holzem et al., 2014

- a recent review found that more than 500 different organic chemicals have been identified in biosolids around the United States. The compounds that are likely to accumulate in biosolids and could have ecotoxico- logical impacts during land application are commonly lipophilic, hydrophobic, and nonionic. These characteristics make these chemicals particularly persistent and bioaccumulative, and pose a potential risk to the human food chain. Specifically, these chemicals have the potential to affect food production by inhibiting crop growth or the processes important to crop growth or human health directly by bioaccumulating in crops that are consumed by humans and livestock.

Carbamazepine

(Miao et al., 2005)

- Anti convulsive medication- widely used

Structure	Analyte	Abbreviation [CASRN[a]]	Formula and MW[b]	Log K_{ow}
	Carbamazepine	CBZ [298-46-4]	$C_{15}H_{12}N_2O$ 236.10[a]	2.25[c], 2.67 ± 0.38[d]

21-25 tons prescribed annually in Canada alone

Ubiquitous in biosolids

- Detected in 80 out of 84 samples at concentrations ranging from 9 to 6030 ug kg^{-1}
- Median biosolids concentration → 94.3 ug kg^{-1} (Sabourin et al 2012)

Kumar Rule of Three

which states that greater absorption and higher permeability of TOrCs is likely when its Log Kow is <3, molecular weight is <300, H-16 bond donors are <3, and H-bond acceptors are <6

Drug Name	Log Kow	OH+NH	MW	N+O	Poor Absorption Alert[1]	Reported Plant Uptake
Carbamazepine	3.53	2	236	3	No	Yes

Log Kow<3

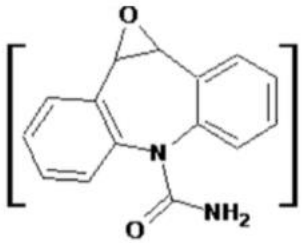
MW<300

H-Bond Donors <3

H-Bond Acceptors <6

Basics

- Dibenzadiozepine derivative
- Chronically administered
  - 100-2000 mg daily
  - <3% of administered dose is excreted in parent form
  - 10,11 – expoxycarbamazepine primary metabolite

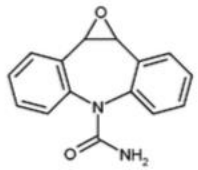
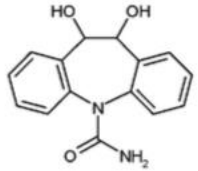
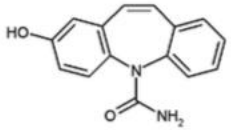
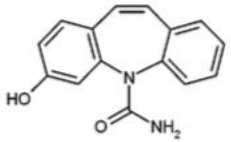
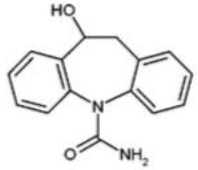


[10,11-epoxycarbamazepine]

Metabolites

(Miao et al., 2005)

- Partial degradation products

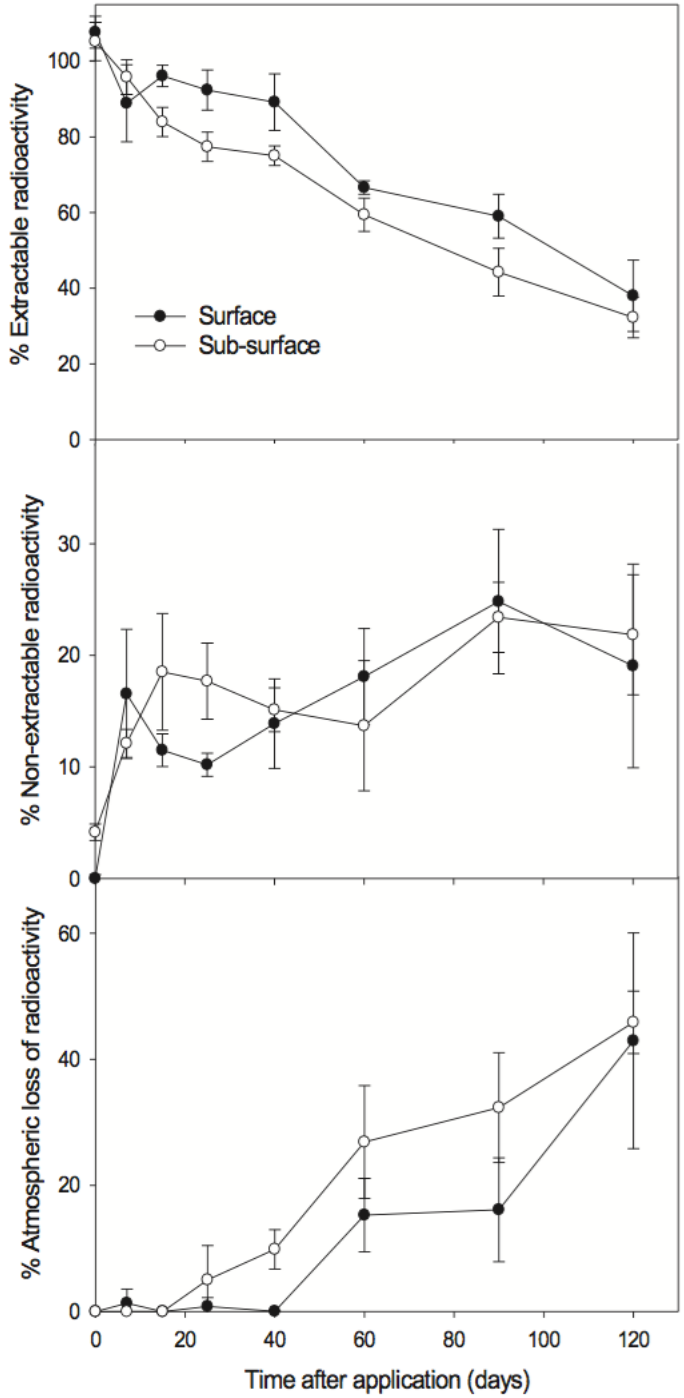
	10,11-dihydro-10,11-epoxycarbamazepine	CBZ-EP [36507-30-9]	$C_{15}H_{12}N_2O_2$ 252.09	1.26 ± 0.54^{d}
	10,11-dihydro-10,11-dihydroxycarbamazepine	CBZ-DiOH [35079-97-1]	$C_{15}H_{14}N_2O_3$ 270.10	0.13 ± 0.41^{d}
	2-hydroxycarbamazepine	CBZ-2OH [68011-66-5]	$C_{15}H_{12}N_2O_2$ 252.09	2.25 ± 0.65^{d}
	3-hydroxycarbamazepine	CBZ-3OH [68011-67-6]	$C_{15}H_{12}N_2O_2$ 252.09	2.41 ± 0.73^{d}
	10,11-dihydro-10-hydroxycarbamazepine	CBZ-10OH [29331-92-8]	$C_{15}H_{14}N_2O_2$ 254.10	0.93 ± 0.33^{d}

Behavior in biosolids- Dissipation rate- DT_{50}

- Rates reported in literature
- Dalkmann et al. (2014)
  - 355- 1 624 days
- Walters et al. (2010)
  - 462-533 days

Rajab et al., 2015
DT_{50} 74.5-97.6

- Cores incubated in experiment station in England
- Initial concentration 10 ug g^{-1}



Plant uptake has been observed

- Wu et al., 2015
  - Detected plant uptake in
    - Root (153 +/- 46 ng g^{-1})
    - Stem (27.3 +/- 0.3 ng g^{-1})
    - Shoot (216 +/- 75 ng g^{-1})
  - For soybean grown in biosolids amended soils

Negative Impacts on Plant Growth

- Carter et al., 2015
  - Detected leaf burn in zucchini when soil concentrations of carbamazepine > 4 ppm
  - Also observed changes in plant hormone balances when carbamazepine > 4ppm in soil

High Hazard Potential

- Slow degradation rate coupled with observed plant uptake indicates that carbamazepine in biosolids amended soils is a significant concern and potential risk

Risks in Perspective

- Carbamazepine is not a new drug
- Carbamazepine was discovered in 1953 by Swiss chemist Walter Schindler.[6] It was first marketed in 1962.[7] It is available as a generic medication and is not very expensive.[8] It is on the WHO Model List of Essential Medicines, the most important medications needed in a basic health system.[9]

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Concentrations in biosolids amended soils- do the math

- 0.0943 mg/kg median concentration in biosolids
- High rate application scenario → biosolids compost (2:1 blend sawdust: compost by volume) added to soil at 2:1 soil: biosolids compost, also by volume)
- 0.0021 mg/kg in finished topsoil at time = 0, about half that concentration after 1 – 2 years
  - 0.137 mg/kg at the highest reported concentration in biosolids in this high application rate scenario

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Wu et al

- The soil had 44 ppm Carbamazepine- you can't even find that in pure biosolids
  - This is 320 x the soil concentration from our high application rate/high carbamazepine concentration scenario
  - Or, **20,500 x** the soil concentration from our high application rate, but more typical carbamazepine concentration
- And those soybeans- the results for the beans, the parts that people eat- were non detect

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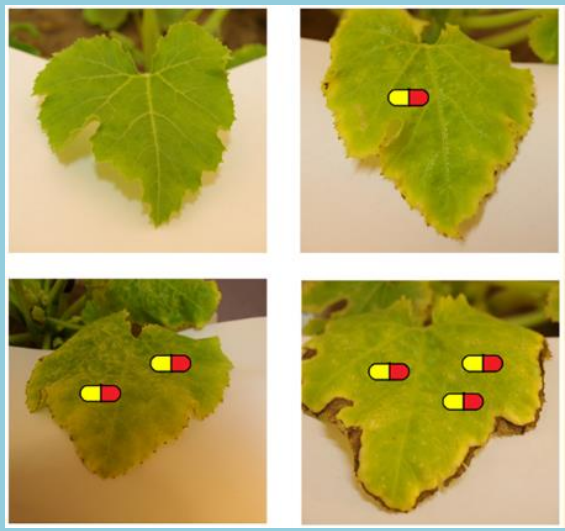
Closer look at the zucchinis



- No biosolids added to the soil, just the drug (possibly therapeutic?)
- Possible similar limitations to spiking soils with metal salts
  - No increase in soil organic matter → increased adsorption of carbamazepine has been documented in biosolids-amended soils (Williams et al 2006)

- Actual zucchinis grown in biosolids-amended soil

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Studies with real biosolids

- Sabourin et al. 2012 looked at garden vegetable (tomatoes, potatoes, carrots and sweet corn) uptake after biosolids had been applied
- Gottschall et al., 2012 added biosolids to wheat fields and analyzed wheat grain
- THERE WAS NO EVIDENCE OF PLANT UPTAKE OF CARBAMAZEPINE UNDER THESE MORE REALISTIC CONDITIONS

They just see growth- explosive growth

And how about the other benefits

- **Increased soil organic matter**
- **Healthier/more robust soil ecosystem**
- **Increased carbon sequestration**
- **Slow –release nutrients**
- **Eliminating the need for purchased commercial fertilizers**
- **Cleaner water**

Even unrealistic scenarios result in exposures that are orders of magnitude lower than therapeutic doses (Wu et al., 2015)

- Based on hydroponic experiments… estimated an individual's annual exposure to PPCPs for average daily consumption of leafy vegetables, and the estimated annual exposure values ranged from 0.04 to 350 µg for an average, 70-kg individual residing in the United States. These estimates of annual exposure were much smaller than that expected in a single medical dose (typically in the 200 - 400 mg range for adults with epilepsy).
- It would take 570 years of eating these vegetables from the highest concentrations found under hydroponic conditions to get the low-end of daily therapeutic dose of carbamazepine
- This is based on a hydroponic experiment in which carbamazepine was added directly to water in which plants were growing.

Concluding Remarks

- It is important to look at research related to biosolids with a critical eye
- The mere presence of compounds in biosolids does not signify risks
- Historically, experimental conditions investigating the presence, fate and transport of potential contaminants in biosolids have often been based on laboratory conditions that are not relevant to actual soil conditions
- Constituents found in biosolids are a mirror of compounds that we use extensively in contemporary society, but our potential exposure to these compounds through the use of biosolids as a soil amendment is often several orders of magnitude lower than our exposure in other typical settings