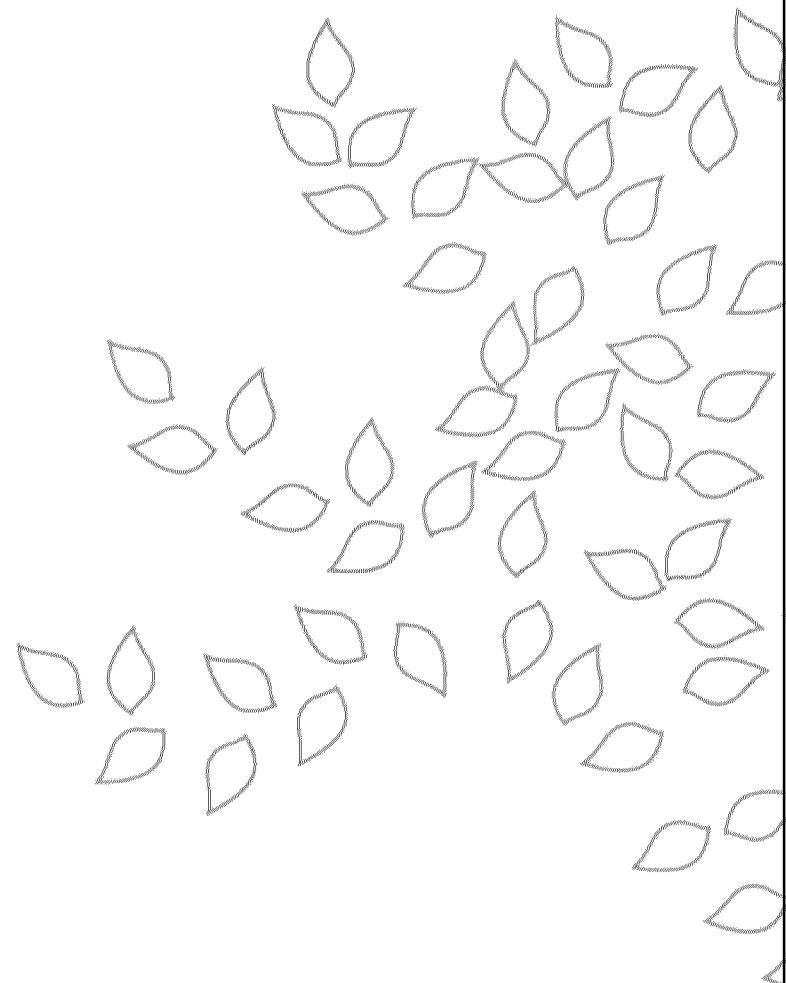




Gramoxone INTEON® - Introduction in Technology

Updated version Jan. 2007, Roland Dieterle



Paraquat history

- Herbicidal properties discovered in 1955
- Introduced in Malaysia and UK in 1962
- Quickly gained acceptance in plantation, tree line and inter-row spraying
- Research into no tillage, minimum tillage and direct drilling in 70's lead to significant impact on agriculture
- Perfect fit for farming – reducing the level of tillage in fragile soils and in rotation with glyphosate to prevent resistance



Paraquat history (cont)

- Registered and sold in 70 crops in 120 countries worldwide
- Used by millions of farmers around the world for over 40 years with excellent occupational safety record
- At times paraquat is misunderstood in regards to user safety, environmental impact and general performance



The importance of paraquat to farming

- Soil erosion is responsible for 40% of land degradation worldwide
- Soil erosion reduces when soil structure improves
- The use of paraquat in combination with reduced tillage
 - Improves soil structure
 - Improves organic matter content
 - Improves water holding capacity
- Paraquat is used as an effective resistance management tool (add slides on development of glyphosate resistance in your country and PQ as viable option, if available)



The INTEON® project

- Paraquat formulations are known to
 - offer excellent weed control in a broad range of crops
 - be safe in occupational use
 - be irritant to skin and eye
 - be toxic by ingestion
- Syngenta has undertaken research to improve existing products for many years
- The INTEON® project emerged out of a broader research programme in 1997 to reduce the acute toxicity of paraquat
- INTEON® is based on a novel formulation technology using alginates



The INTEON® project (cont)

- Utilises an alginate gelling agent, emetic and purgative to reduce absorption of paraquat into the body
- Breakthrough formulation technology
- A new safety standard for paraquat formulations



Alginates

- Carbohydrates of polymannuronic and polyguluronic acid
- Non-toxic
- Commonly used in the food industry as gelling agents eg ice cream, toothpaste
- Used in the pharmaceutical industry for their therapeutic properties, in treating dyspepsia, and in wound healing eg Gaviscon antacid



Background to INTEON®

- Paraquat is much more readily absorbed from the small intestine than either the oesophagus or the stomach
- The alginic acid is soluble in water at neutral pH. However in the acid environment of the stomach (pH 2) it rapidly forms a gel
- The stomach reacts to bulk (in this case the gel) releasing the hormone gastrin which releases acid and closes the pylorus, thereby delaying emptying of the stomach into the small intestine

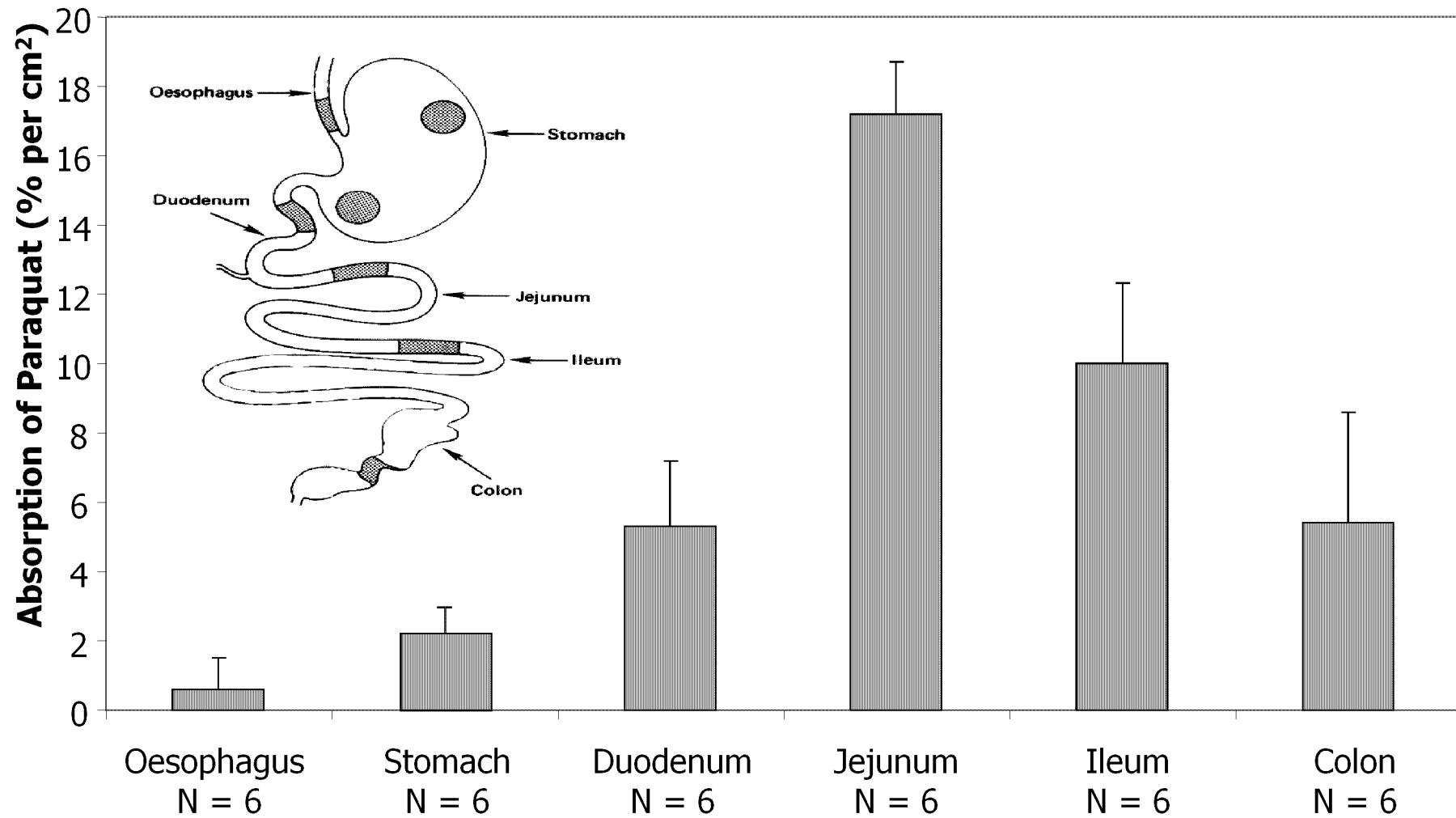


Background to INTEON® (cont)

- PP796 is an effective emetic that acts in the vomit centre of the brain via inhibition of phosphodiesterase. PP796 also closes pylorus and pushes paraquat up and out via the mouth after 15-20 minutes
- Magnesium sulphate ($MgSO_4$) is an osmotic purgative that clears the bowel by stimulating the osmoreceptors in the duodenum. $MgSO_4$ also closes the pylorus and draws water from the body and the bowel to purge any paraquat reaching the bowel
- Effect is like swallowing sea water (purgation and vomiting)



Paraquat absorption from the gastrointestinal tract



Objectives of INTEON® technology

- Prevent paraquat reaching small intestine
 - Retain in stomach and promote rapid emesis
- Reduce residence time for any paraquat that gets through to small intestine
 - Purgation

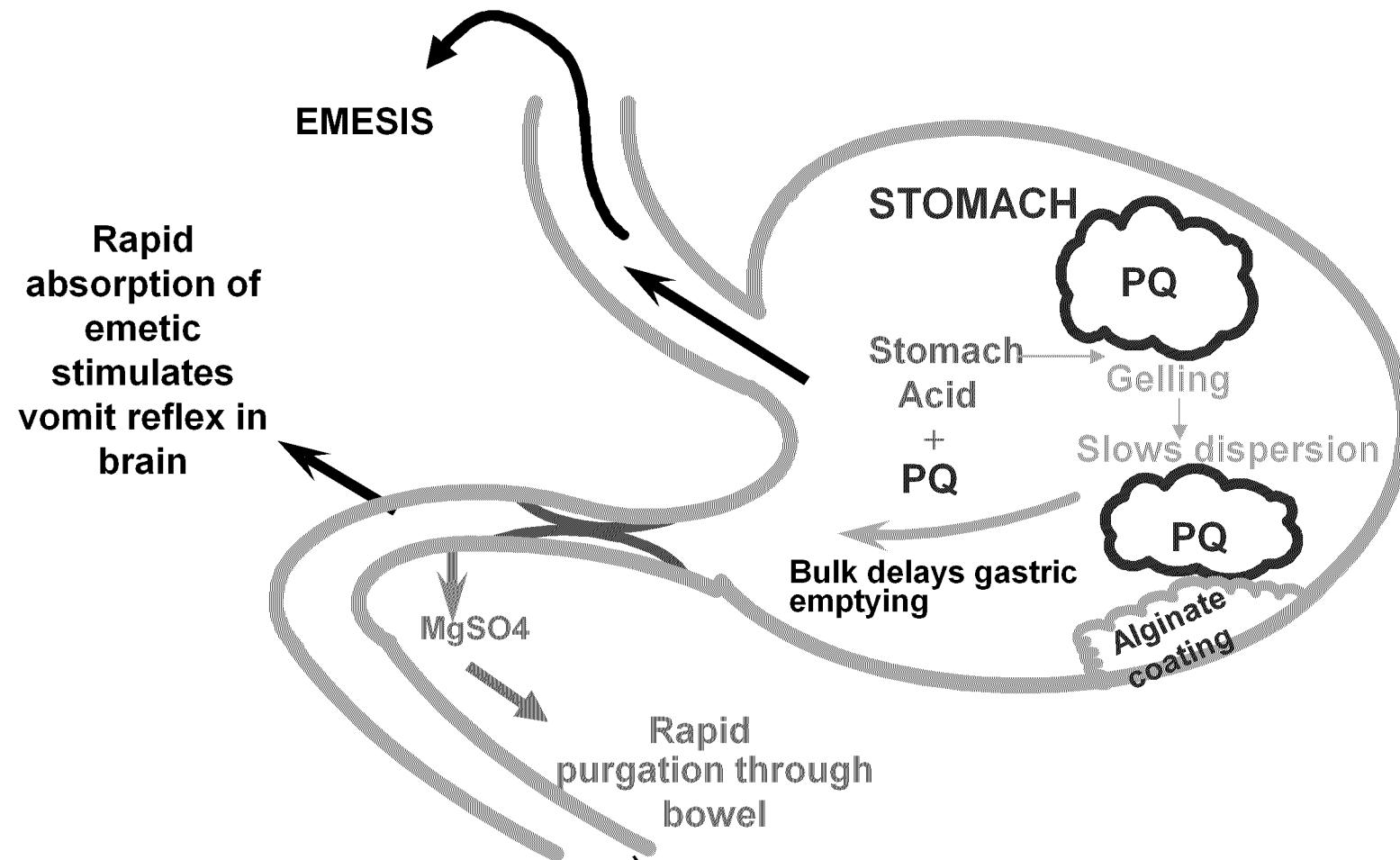


INTEON® technology – the hypothesis

- The alginate will form a gel in the acidic environment of the stomach, slowing the delivery of paraquat to the absorptive small intestine
- The emetic will give more productive emesis since the gelled formulation remains in the stomach longer
- The addition of a soluble purgative agent, magnesium sulphate, should remove any ingested paraquat that has reached the small intestine
- The 3 processes - gelling, emesis and purgation – would in their own right reduce the oral absorption of paraquat. Together they would act synergistically and will reduce the toxicity in a vomiting species following oral ingestion



INTEON® and gastrointestinal physiology



User benefits of INTEON®

- Gramoxone INTEON® sets a new safety standard in paraquat formulations
 - A Gramoxone Observational Monitoring Survey in Sri Lanka has shown that INTEON® technology significantly improves the survival of patients following paraquat ingestion. The survey will continue in 2007.
<http://www.evosof.com/asiatox/tox/5th%20Congress%20of%20APAMT%20-%20Abstract%20book.pdf>
 - Less irritant to the skin and eye
- Expectation that INTEON® formulations will eliminate fatalities from mistaken ingestion
- More user friendly product
- Equivalent efficacy to old formulation and in some instances slightly improved efficacy

