

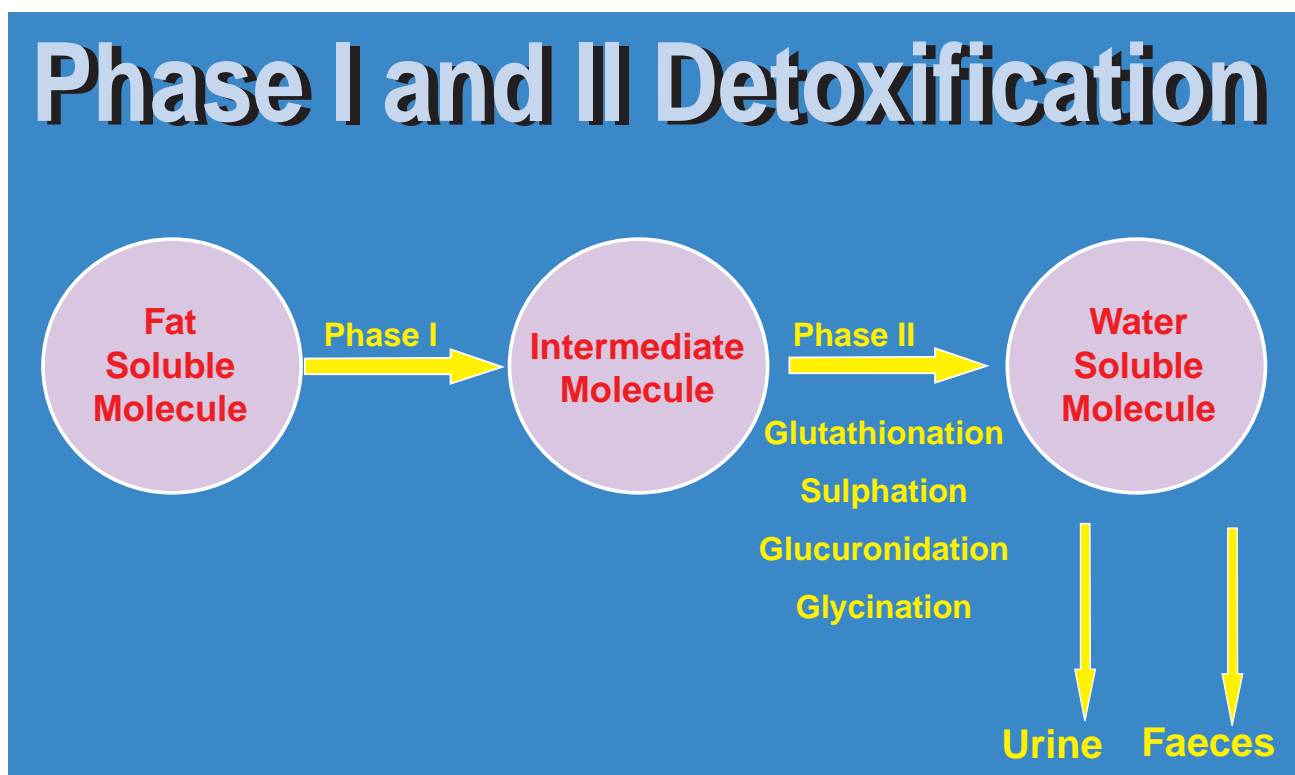
# Functional Liver Detoxification Profile (FLDP)

## Phase 1 Interpretation (Caffeine Clearance)

The Cytochrome P450 enzymes are the predominant enzyme system involved in Phase I liver detoxification. Their role is to convert toxic substances into more water-soluble molecules, so they can be further metabolised in Phase II.

Result	Possible Cause	Treatment Considerations
High Phase 1	Excessive Cytochrome P450 induction from exposure to: Alcohol, nicotine, caffeine, stress Drugs (steroids, sulphonamides, barbiturates, HRT) Toxins (exhaust fumes, paint fumes, dioxin & organo-phosphorous pesticides) High protein diets	Naringenin (grapefruit juice) St Mary's thistle Antioxidants (A, C, E, Zn, Se)
Low Phase I	Reduced activity of Cytochrome P450 from exposure to: Drugs - benzodiazepines, antihistamines, ketoconazole, H2 blockers	Green tea (catechins) Turmeric B group vitamins Bioflavonoids Glutathione & its precursors (glycine, glutamine, cysteine)

## Liver Detoxification Pathways



©ARL Pathology 2005

## Intermediate Phase Interpretation

When Phase I activity is high, there is increased metabolic activity at the intermediate phase (before the molecules are presented to Phase II for conjugation). This results in an increased production of free radicals and the potential for secondary tissue damage. It is therefore essential that adequate antioxidants are available to counteract this high free radical activity.

### Treatment Considerations for the Intermediate Phase:

Vitamins A, C and E, Co-Enzyme Q10, Zinc and Selenium.

## Phase II Interpretation

Phase II reactions involve the addition of a small polar molecule, a conjugation step that may or may not be preceded by Phase I. Several types of conjugation reactions occur in the body, including glutathionation, sulphation, glucuronidation and glycine conjugation. These reactions require nutrient cofactors, which are essential for proper detoxification.

When a Phase II conjugation pathway result is at the **low** or **high** end of the reference range, the requirement for the conjugating amino acid(s) is increased in order to maintain the function of that pathway. Treatment considerations for high and low results are therefore similar.

Pathway	Responsible for Conjugation of:	Treatment Considerations
<p><b>Glutathionation</b> A significantly used pathway which is dependant on the tripeptide (cysteine, glutamine, glycine). Individuals with diagnoses of arthritis, diabetes, or heart disease may have lower glutathione levels than those who are disease free.</p>	<p>Pesticides Paracetamol Toxic Metals e.g. Hg, Cd, Pb Penicillin Tetracycline Petroleum distillates Alcohol</p>	<p>Precursors to glutathione (cysteine, glutamine, glycine) methionine, DIM/cruciferous vegetables, Vitamins B2, B6, C, Selenium, St Mary's Thistle</p>
<p><b>Sulphation</b> It is dependant on a depletable supply of inorganic sulphate. Sulphation is 'rate limited' by the amount of sulphate available to the liver. See Sulphate: Creatinine Ratio. Compensatory mechanism for other Phase II pathways.</p>	<p>Steroid hormones (e.g oestrogens, progesterone, DHEA and melatonin) Phenols (aromatic hydroxyl groups including histamine, dopamine, gallic acid and coumarin) Catecholamines (adrenalin, noradrenalin)</p>	<p>Sulphur-containing amino acids (cysteine, methionine, taurine) Sulphur rich foods Molybdenum (co-factor for sulphite oxidase) Support other pathways as needed</p>
<p><b>Glucuronidation</b> Estimated to account for 33% of all drugs metabolised by Phase II detoxification.</p>	<p>Sex hormones esp. oestrogens Paracetamol NSAIDs Benzodiazepines</p>	<p>Calcium d-glucurate* Magnesium Zinc Curcumin Vitamin B complex Essential Fatty Acids</p>
<p><b>Glycination</b> Predominantly involved in salicylate conjugation.</p>	<p>Salicylic acids e.g. Aspirin Benzoic acids (found in some ointments and food preservatives) Phenylacetic acids (found in nuts and cigarettes)</p>	<p>Glycine Vitamin B6 Magnesium Reduce salicylates</p>

\*Calcium d-glucurate is metabolised to d-glucaro-1, 4-lactone (glucaro lactone GL). GL is a direct inhibitor of beta-glucuronidase, an enzyme found in the gut that cleaves bound oestrogens and carcinogens from their Phase II conjugates and permits reabsorption through the entero-hepatic circulation. By inhibiting beta-glucuronidase activity, GL increases the net elimination of carcinogens, toxins and steroid hormones via glucuronidation.

## Ratios

### Sulphate:Creatinine

This reflects the level of sulphur available from dietary sources and should be considered in conjunction with the Phase II sulphation result.

### Phase I:Glycination and Phase I:Glucuronide

These two ratios reflect the relationship between Phase I and these two conjugation pathways and will demonstrate whether the biochemical load from Phase I is high or low.

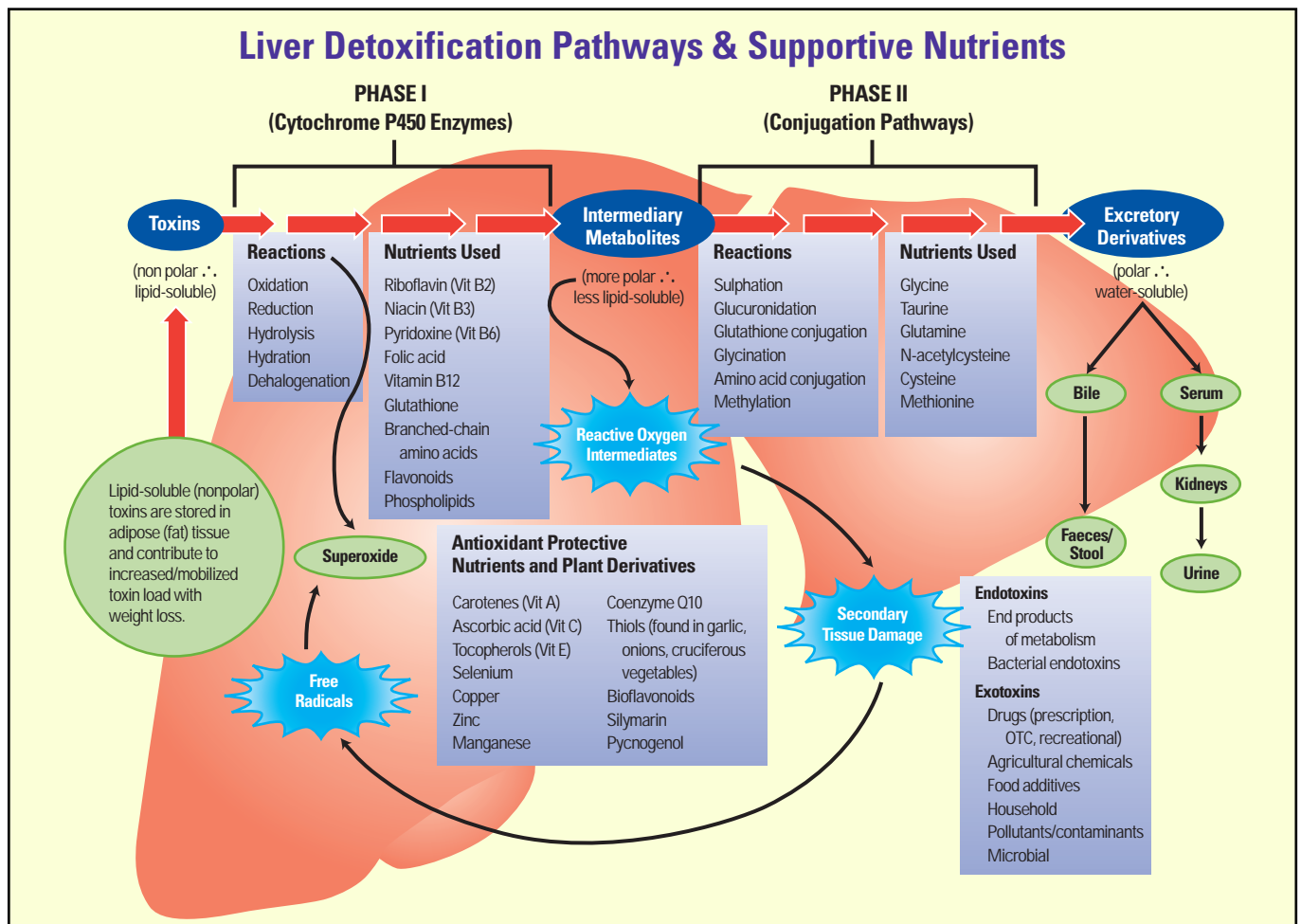
### Sulphate:Glucuronide

This ratio reflects the relationship between sulphate and glucuronide. Sulphate is often up-regulated to compensate for low glucuronide.

### Phase I:Sulphation

This reflects the relationship between Phase I and the sulphation pathway and demonstrates whether the biochemical load from Phase I is too high.

**Note:** When all the ratios are high in an FLDP report, this commonly reflects a patient who is highly sensitive and may have multiple food and chemical sensitivities.



Source: Liska, Lyon & Jones, 2005<sup>5</sup>

## References

- J Lab Clin Med 2002;140(6):413-7.
- Bland, J. et al. Clinical Nutrition: A Functional Approach, Washington, 1999.
- Mb Oguro, T. et al. Molbdate Depletes Hepatic 3-Phosphoadenosine 5-Phosphosulphate and impairs the Sulphations of Acetaminophen in Rats, J Pharm & Exp Ther, 1994; 2703: 1145-1151.
- Wallig, M. Toxicol. Sciences, 2004; 78: 1-2.
- Liska, D, Lyon M, Jones DS. "Detoxification and Biotransformational Imbalances" in Textbook of Functional Medicine (Ed-Jone DS). The Institute for Functional Medicine, Gig Harbor USA, 2005.