

B I O S Y N

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Physical Characterization of an Artificial Cervical Mucus

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Project Objectives

- To develop a synthetic cervical mucus formulation that has the physical and chemical properties of fresh mucus
- Evaluate the synthetic formulation using a Brookfield cone and plate viscometer

Composition & Characteristics of Mid-Cycle Cervical Mucus

- Electrolytes (1 - 1.5%)
- Proteins (0.5 - 1.0%)
- Lipids (0.5 - 1.0%)
- Glycoproteins (0.5 - 5%)
- Water (>95%)
- pH = 7.4
- Viscosity - 2,840 to 10,000 cP

Mid-Cycle Human Cervical Mucus

- Inconsistent availability
- Poor yield
- High variability from subject to subject
- Fast degradation

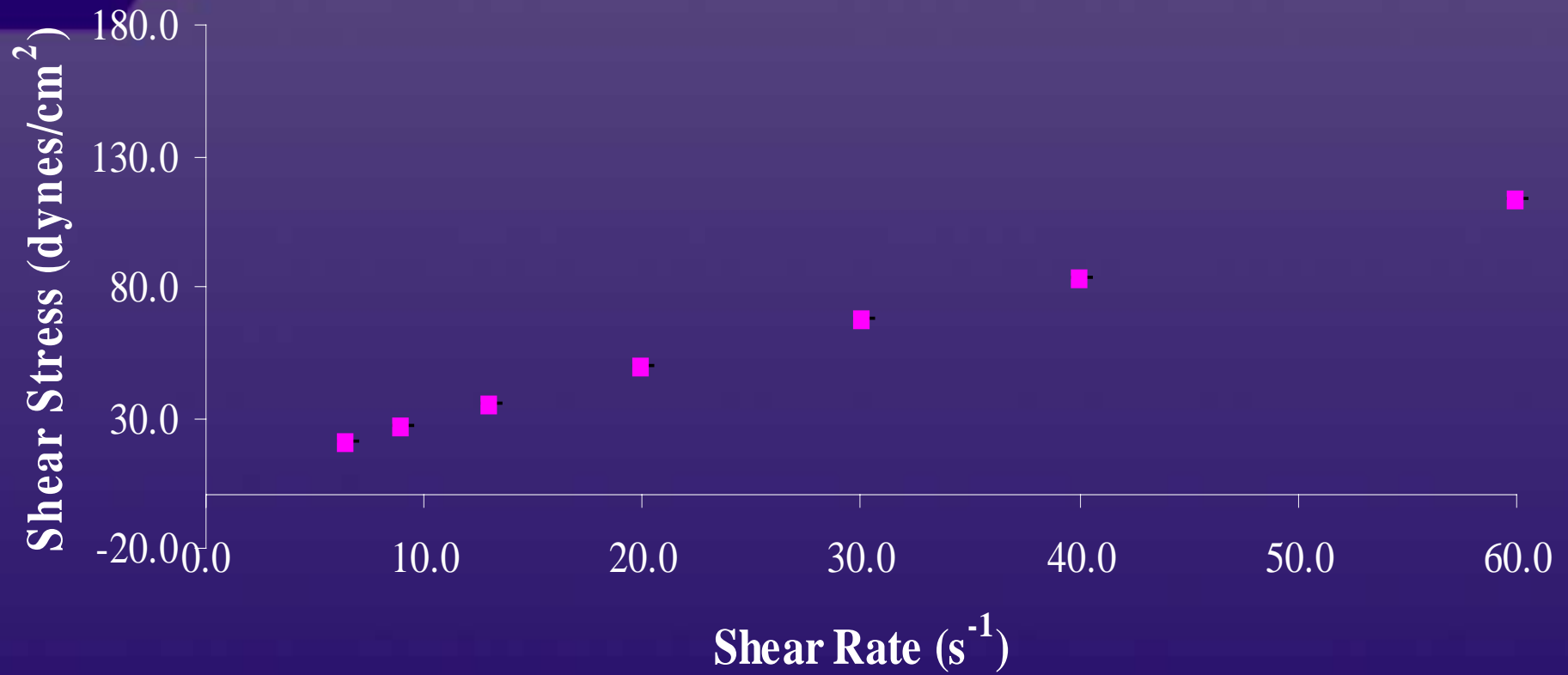
Several Mucus Substitutes

- Guar gum
- Hyaluronic acid
- Acrylamide
- Mixtures of polyethylene and acrylamide
- Hen egg whites

Initial Mucus Formulation

- 1.0% guar gum
- 0.1% sodium azide (preservative)
- 0.1M potassium phosphate buffer
- Water to make up 100%

Viscosity Profile: Initial Guar Formulation

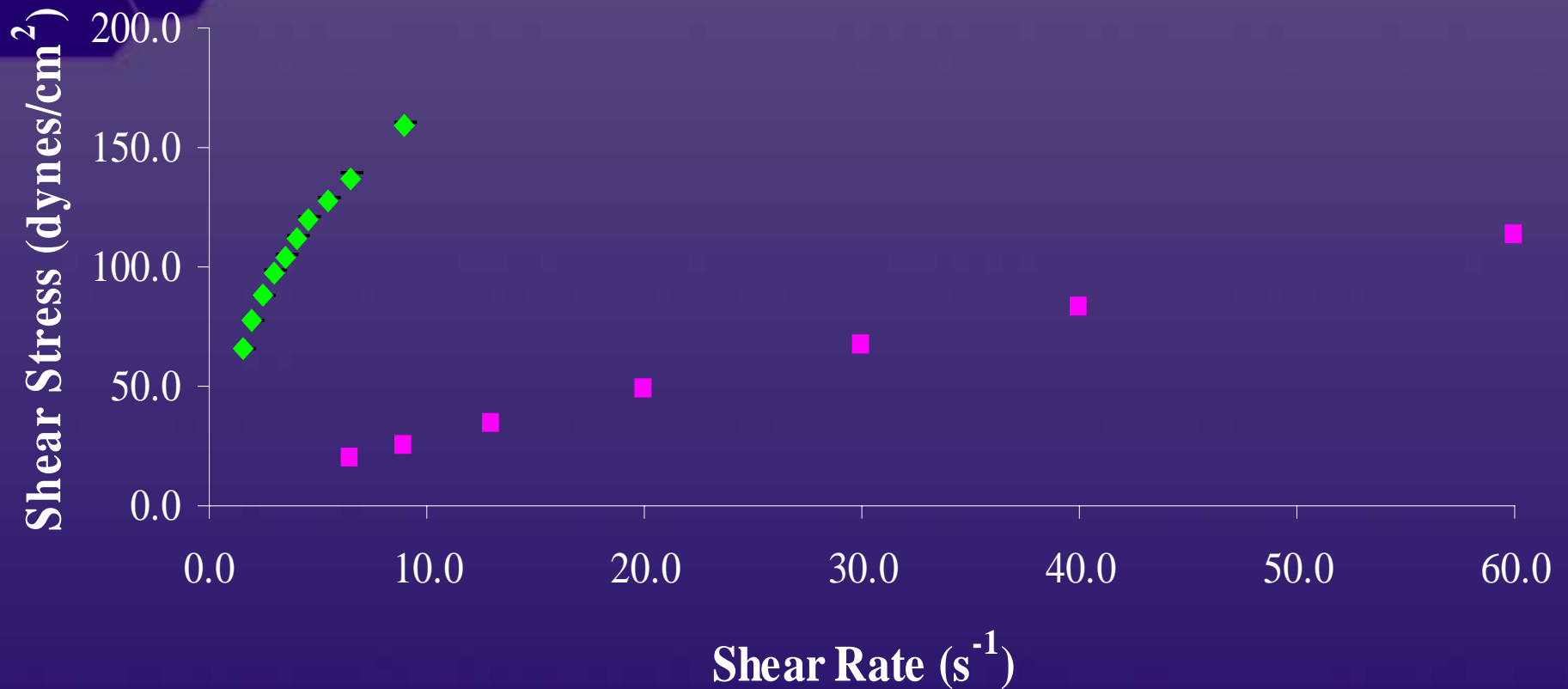


Apparent Viscosity is 283 cP at 9 s⁻¹

Important Factors: Synthetic Cervical Mucus Formulation

- Process
 - gum needs time to hydrate prior to addition of other potential interactive species
- Mucin
 - necessary for representation of glycoprotein fraction of mucus
- Preservative
 - interactions are possible, must be investigated
- Guar Gum Source
 - Determine if guar gum source has an impact on the viscosity of the formulation

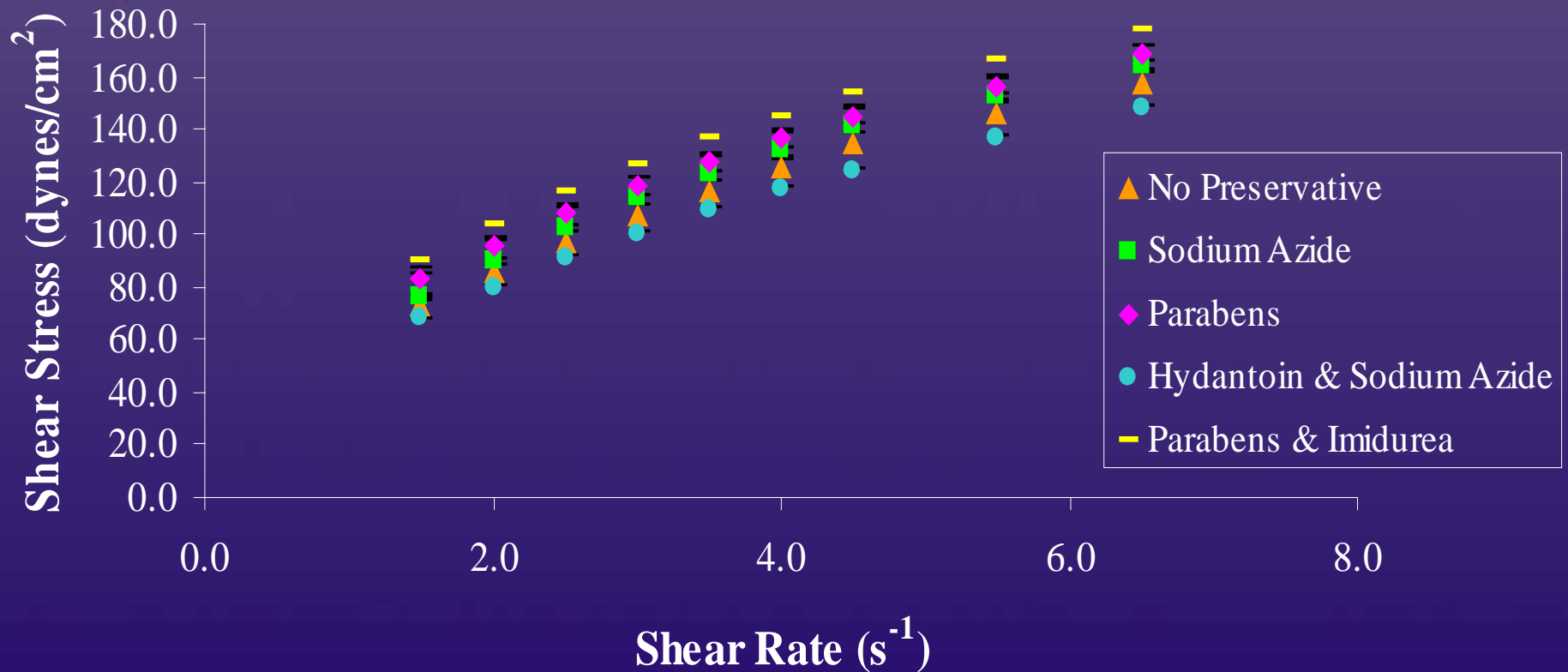
Process: One Step vs. Extended Hydration



Apparent viscosity at 9 s⁻¹;

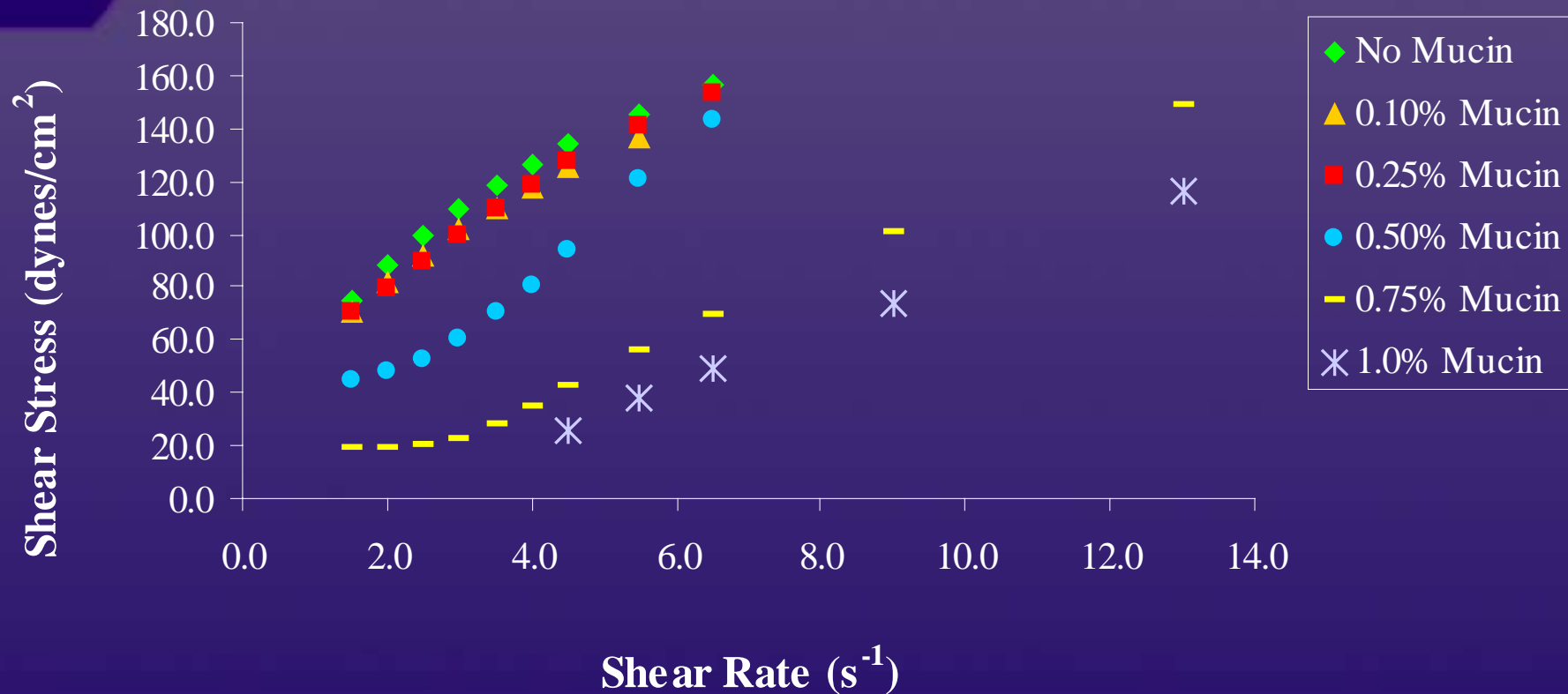
One Step Hydration (♦) = 283 cP, Extended Hydrated (■) = 1765 cP

Preservative: Identifying the Right System



Viscosity comparison for several preservative systems

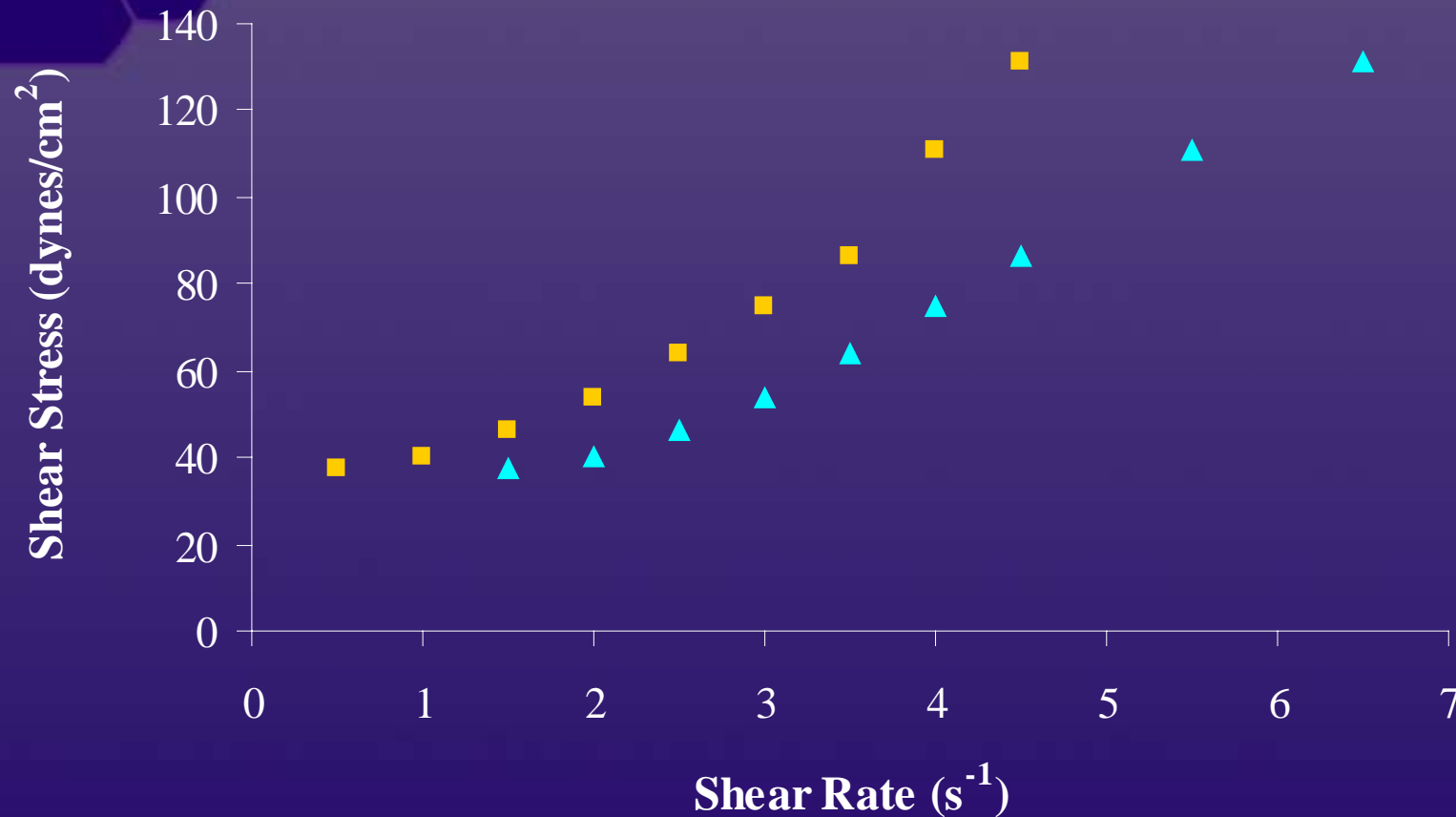
Mucin: Incorporating Glycoprotein Fraction



Apparent viscosity at 4 sec⁻¹:

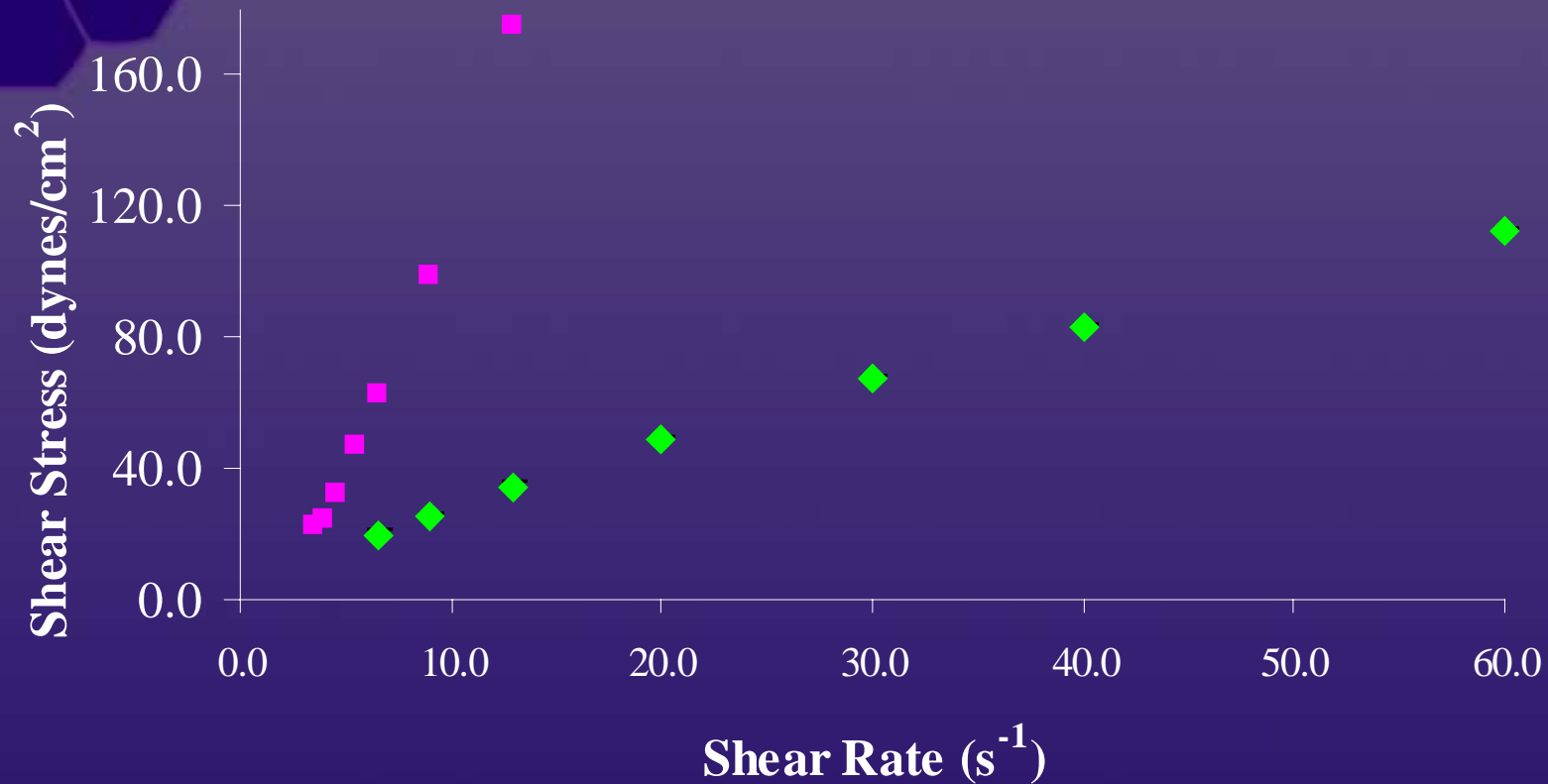
No mucin = 3306 cP, 0.1% mucin = 4240 cP, 0.5% = 2276 cP

Guar Gum Source Comparison



At 1.50 s⁻¹, Hercules Guar (■) = 3,477 cP, Sigma Guar (▲) = 2,469 cP.

Comparison between Initial Formulation & Modified Formulation



Apparent viscosity of initial formulation (?) = 306 cP (at 6.5 s⁻¹)

modified formulation (◆) = 4240 cP (at 4 s⁻¹)

Other Characteristics of Mucus

- Spinnbarkeit:
 - Subjective measure of the rheological properties of mucus
 - Borate concentration was adjusted to have spinnbarkeit
- Osmolality:
 - Measure of the number of small particles in a kg of solvent
 - Human physiological fluids = 275-295 mOsm/kg
 - Synthetic cervical mucus = 272 ± 6 mOsm/kg

Final Formulation: Synthetic Cervical Mucus

- 1.00% guar gum
 - 0.50% porcine gastric mucin (type III)
 - 0.15% methylparaben
 - 0.02% propylparaben
 - 0.30% imidurea
 - 0.1M pH 7.4 potassium phosphate buffer
(0.26% KH_2PO_4 & 1.57% K_2HPO_4)
 - Water to make up 100%
- 0.1M sodium borate solution as a crosslinker

Conclusions

- A synthetic cervical mucus has been developed that has similar viscosity, mucin content, osmolality and spinnbarkeit to that of fresh mucus, as reported in literature.
- The synthetic formulation maintains its physical properties for a minimum of one month at room temperature.