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“Measure Often, Produce Once:”

A case study of the effect of binder type on dry granulation and tablet compression properties in a model formulation

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Purpose

To compare the impact of roller compaction processing parameters and resulting tableting properties using dry granulation binders.

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Methodology

- Model formulation with four components :
  - API (30% drug load),
    Disintegrant (Crospovidone)
    Binder: 1) Avicel® DG, 2) Avicel PH 101 + Di-calcium phosphate, 3) Kollidon® VA-64 Fine
    Lubricant (Magnesium stearate)

- Roller compaction processing parameters (varied):
  - Ribbon thickness, roller force, roller speed

- Roller compaction parameters (not varied):
  - Mill speed (90 rpm) and granulator screen (0.8 mm)

- Compression force (not varied)

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Formulation

Figure 2: List of Ingredients in the formulation

Ingredients	%w/w	%w/w	% w/w
	Intra-Granular		
Acetaminophen	30	30	30
Mag. Stearate	0.5	0.5	0.5
Crospovidone	3.0	3.0	3.0
Avicel DG	64.0	N/A	N/A
Microcrystalline Cellulose (Avicel PH 101)	N/A	48.0	58.0
Di-Calcium Phosphate	N/A	16.0	N/A
Kollidon VA-64 Fine	N/A	N/A	6.0
	Extra-Granular		
Mag. Stearate	0.5	0.5	0.5
Crospovidone	2.0	2.0	2.0
TOTAL	100	100	100

Roller Compaction
Materials, Parameters, Levels

Materials	Process Parameters	Levels
Avicel® DG [ADG]	Roll Force	6, 12, 18 kN/cm
	Granulator screen	0.8 mm
Avicel® PH-101 and Di-calcium phosphate [PADCP]	Ribbon thickness	2, 3, 4 mm
	Granulator mill speed	90, 120 rpm
Kollidon® VA-64 Fine [KVA 64]	Roll speed	2, 4, 8, 12 rpm

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Manufacturing Process Flow

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Results

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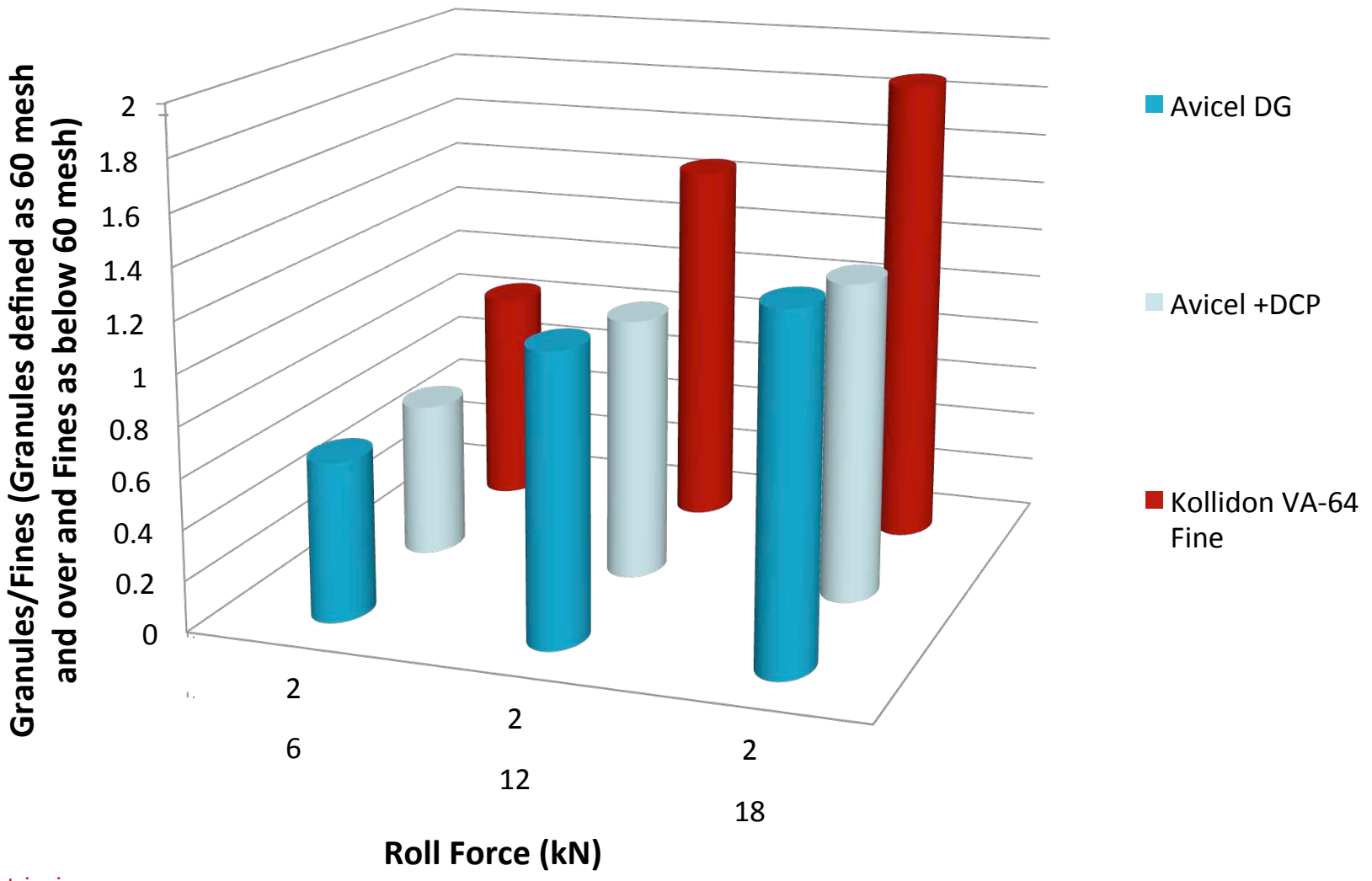
Granules/Fines vs. Roll force at roll gap of 2 mm



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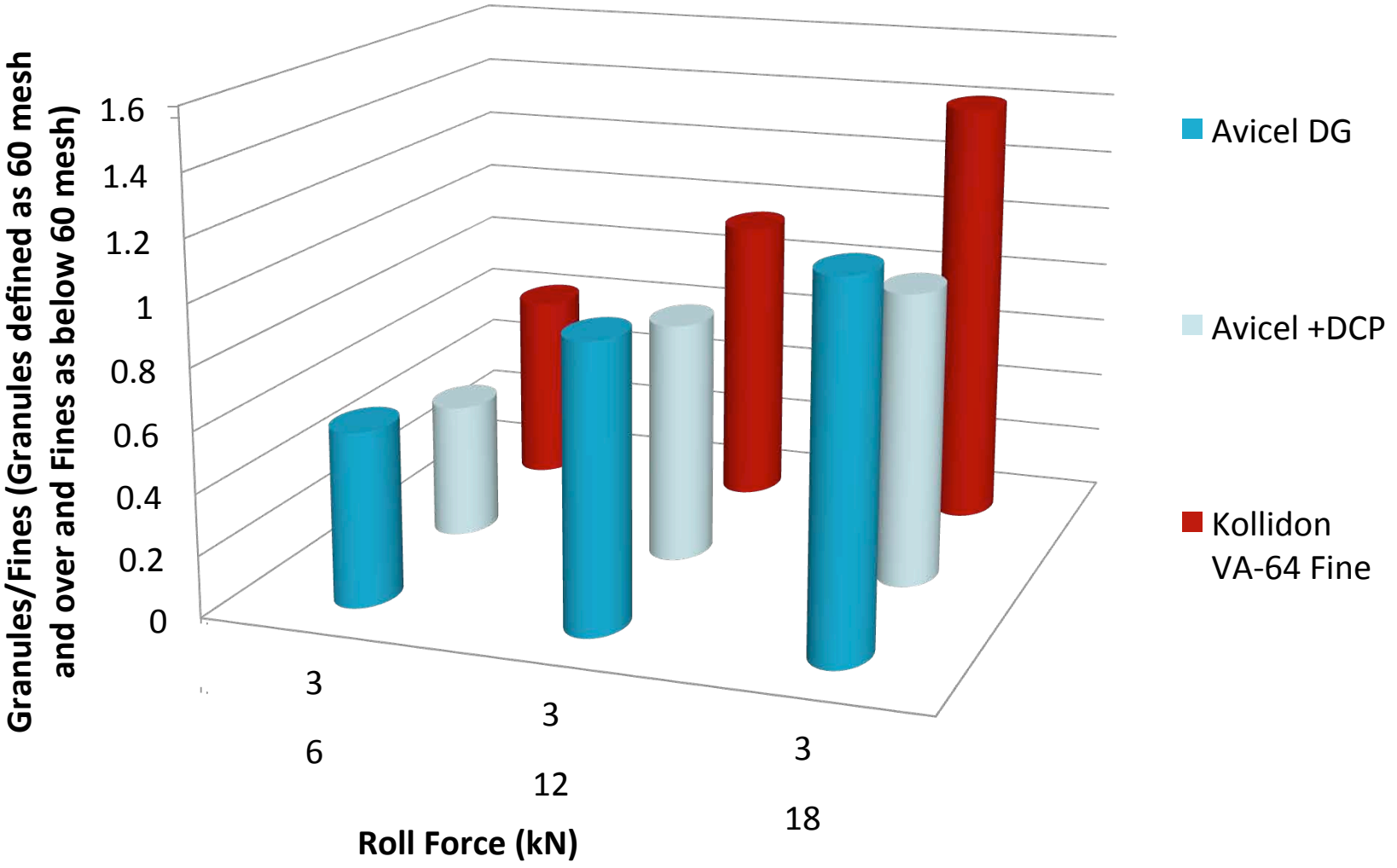
Granules/Fines vs. Roll force at roll gap of 3 mm



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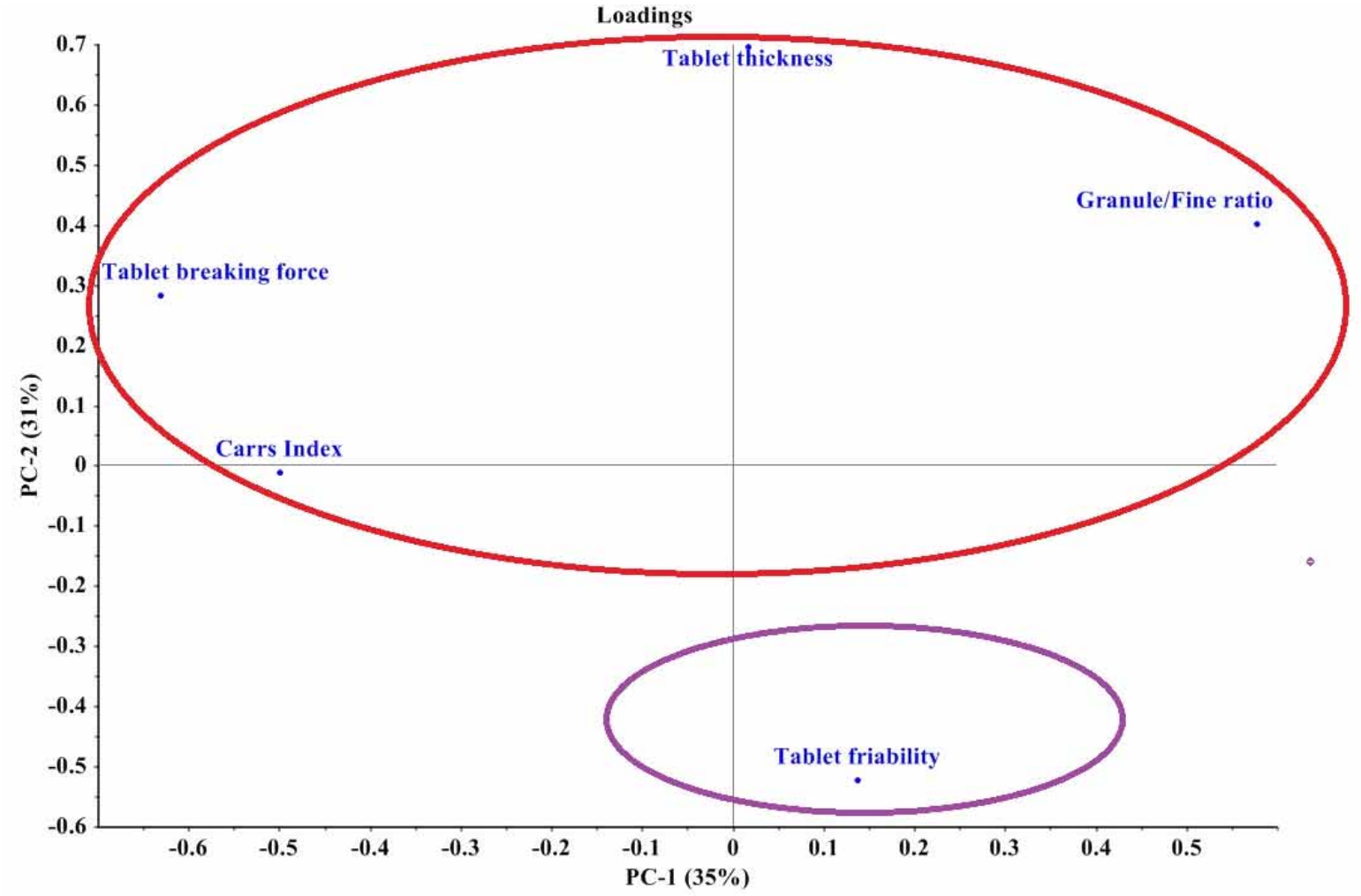
Principle component (PC) analysis – scores plot



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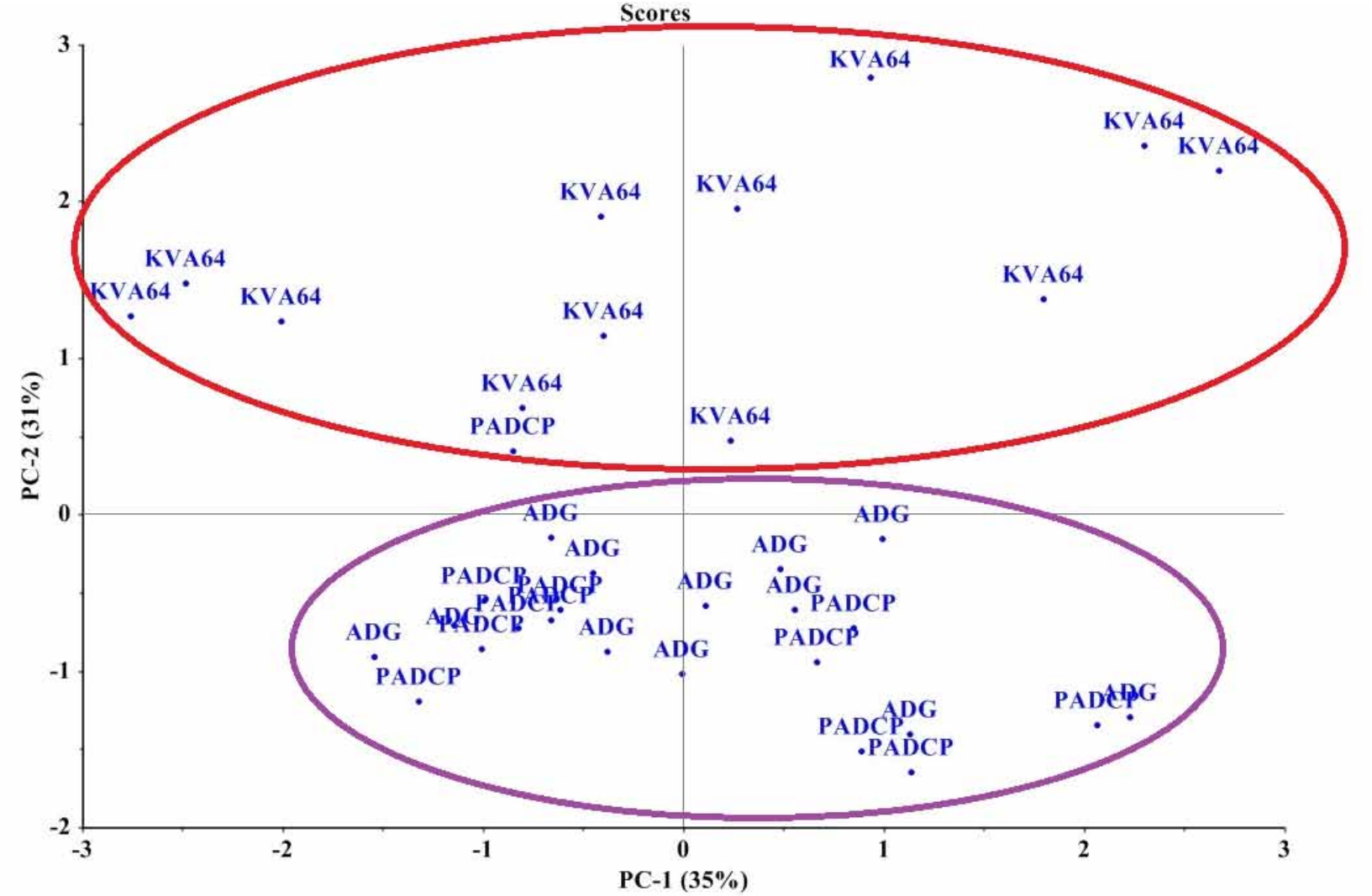
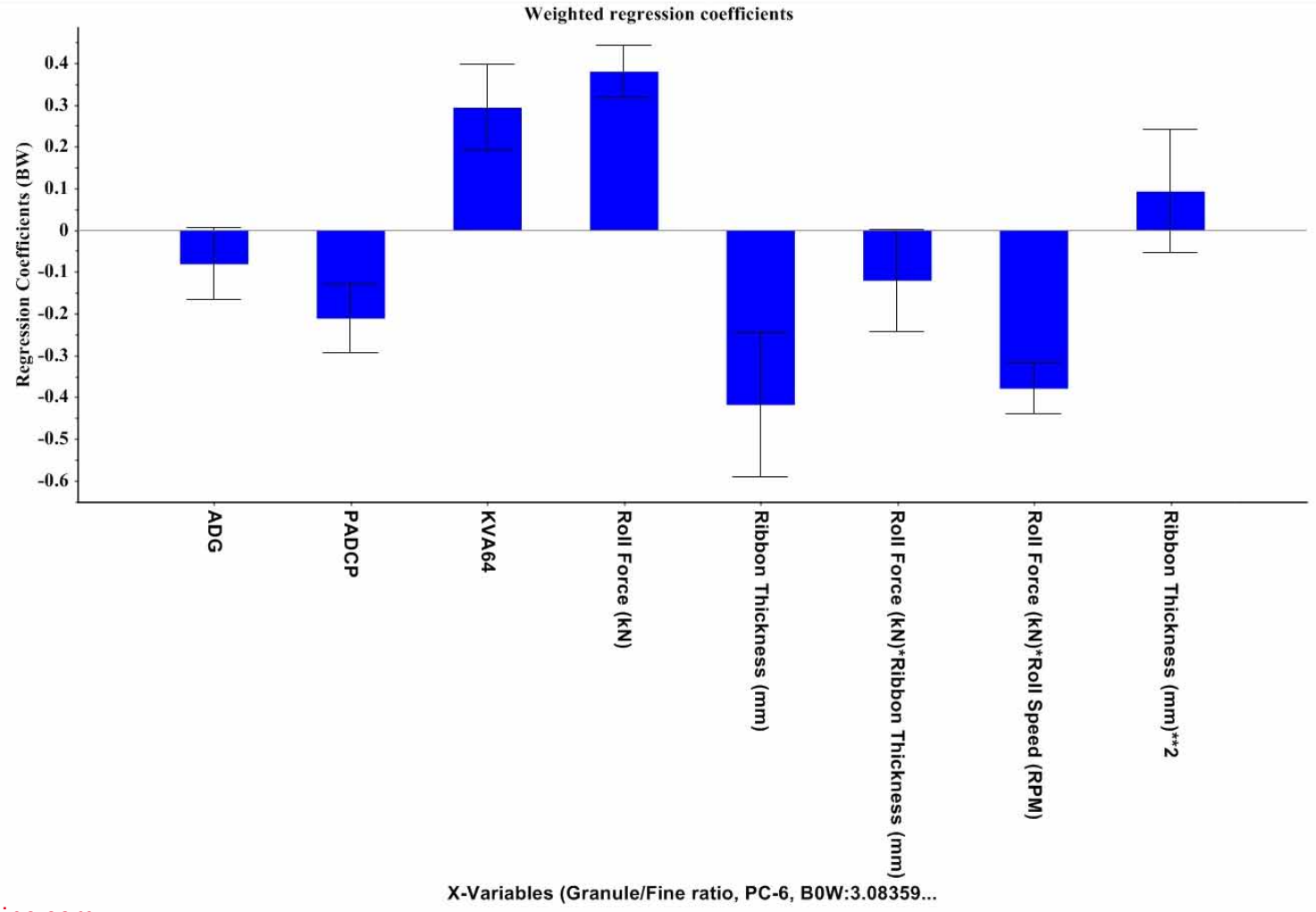
Principle component (PC) analysis - scores plot



Principle component (PC) analysis – loading plot

Granules/Fine Ratio



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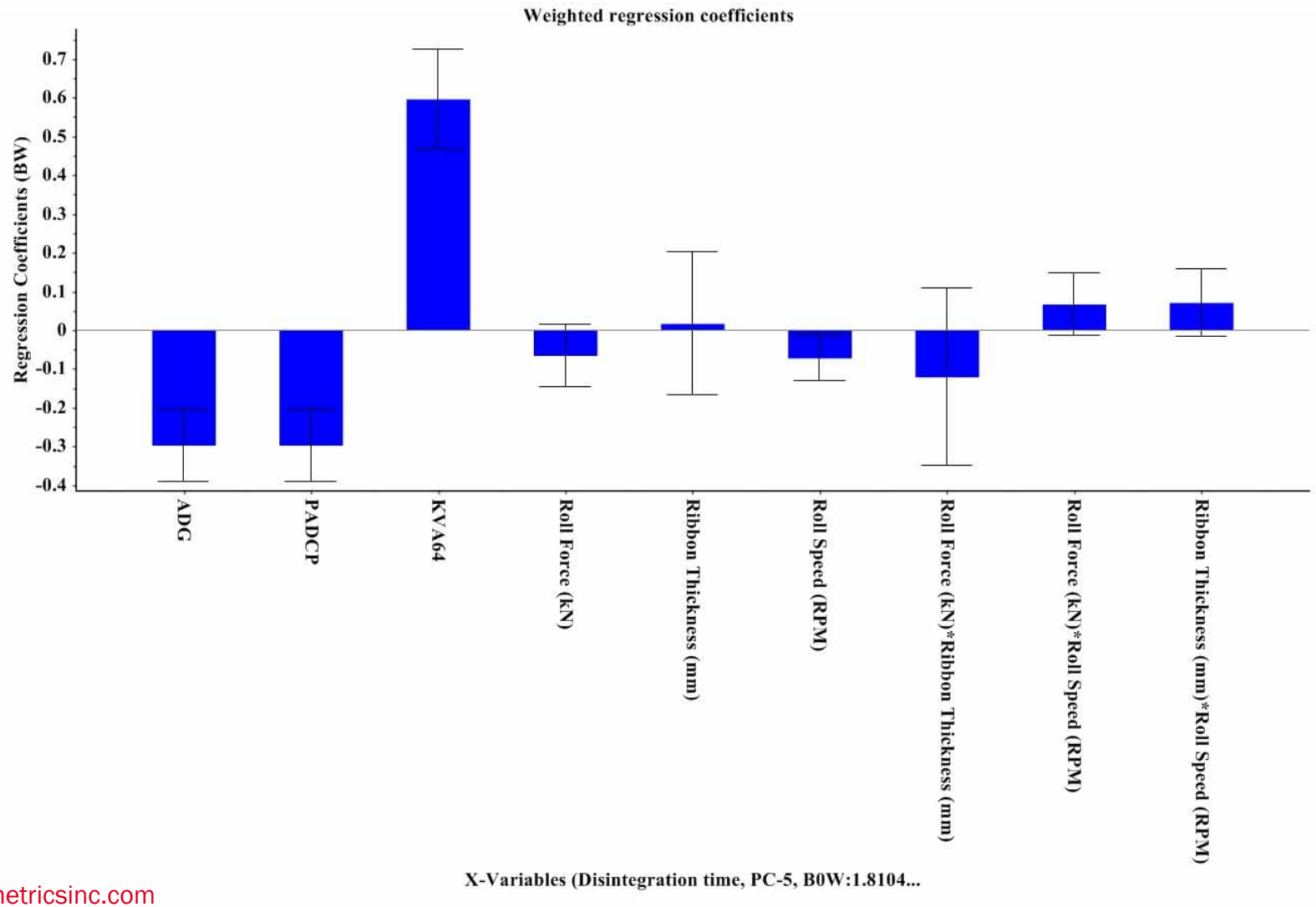
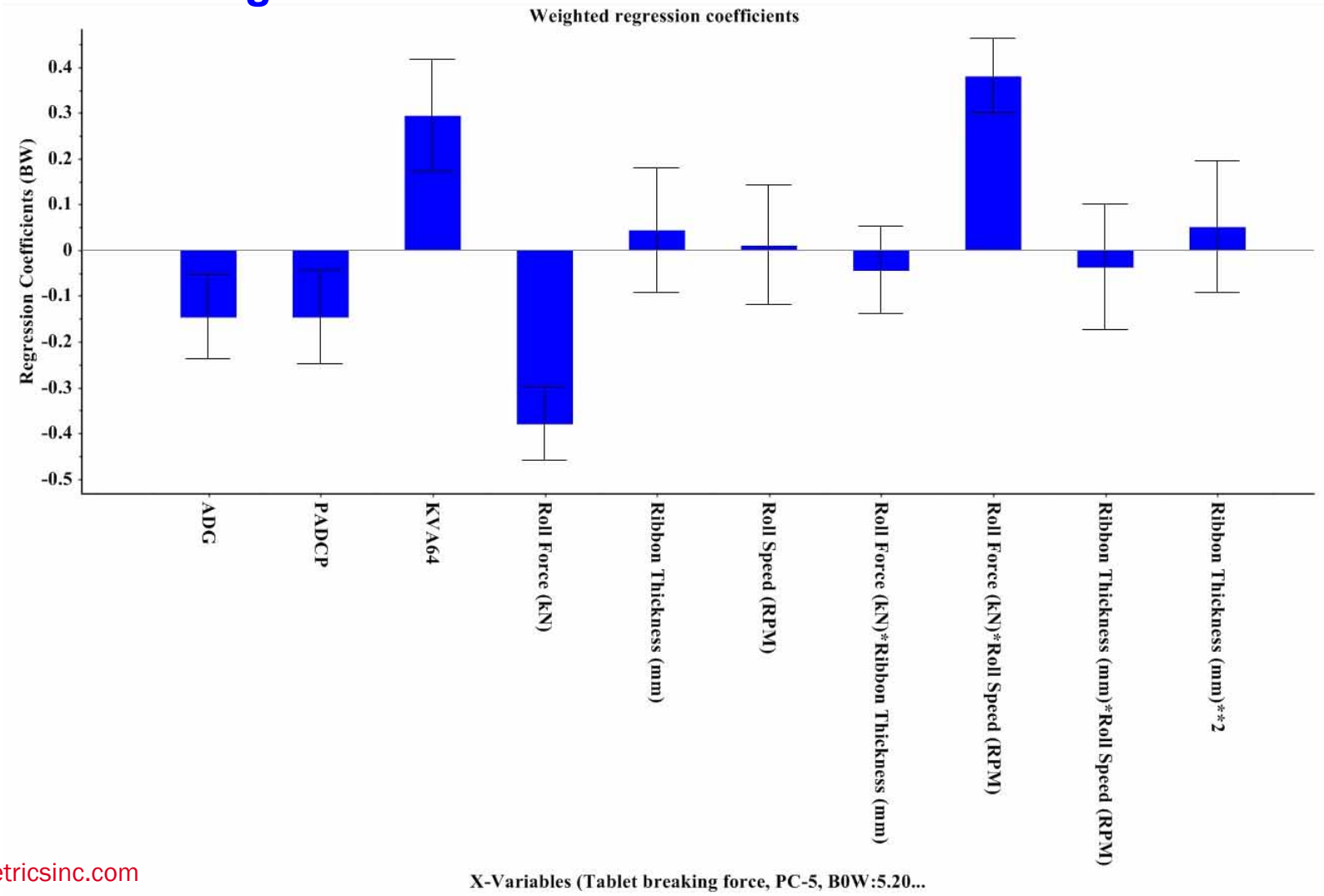
Principle component (PC) analysis – loading plot

Disintegration Time



Principle component (PC) analysis - loading plot

Tablet Breaking force



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Conclusions

- Present investigation showed sensitivity of selected binders to studied design variables and their interaction effects within subjected design space.
- Better granulation and tableting properties can be arranged in following descending order: KVA64 > PADCG > ADG
- KVA-64 fine blends exhibited the highest proportion of granules/fines.
  - Ratio was inversely proportional to the roller gap.

Conclusions

- Tablet hardness was inversely proportional to roller compaction force; the hardest tablets produced used KVA-64 fine blends.

- Study shows value of examining the correlation between a dry granulation binder and the roller compaction parameters in order to create a working design space.

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Questions?